SETTLEMENT AGREEMENT AND MUTUAL RELEASE

This Settlement Agreement and Release ("Agreement") **IS HEREBY STIPULATED AND AGREED TO** by and between Representative Plaintiffs Kate Weissman, Richard Cole, and Zachary Rizzuto (on behalf of themselves and each of the Class Members who have not validly and timely requested to Opt-Out of this Agreement) and Defendants UnitedHealthcare Insurance Company, UnitedHealthcare Services, LLC, Interpublic Group of Companies, Inc., Choice Plus Plan, and The Hertz Custom Benefit Program (together, "Defendants"), by and through their respective counsel. In this Agreement, Defendants UnitedHealthcare Insurance Company and UnitedHealthcare Services, LLC are referred to collectively as "United." In this Agreement, Plaintiffs and Defendants each are referred to individually as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, Plaintiff Kate Weissman filed her original Complaint in this action in the District of Massachusetts on March 26, 2019.

WHEREAS, Plaintiff Richard Cole filed an action in the Southern District of Florida that was transferred to the District of Massachusetts and consolidated with Ms. Weissman's case on April 8, 2020.

WHEREAS, Plaintiff Zachary Rizzuto filed an action in the Middle District of Florida that was transferred to the District of Massachusetts and consolidated with Ms. Weissman's case on April 13, 2020.

WHEREAS, Plaintiffs filed their Consolidated Amended Complaint in this action on May 15, 2020.

WHEREAS, the Parties wish to fully and finally settle the consolidated proceedings in the United States District Court for the District of Massachusetts, including the consolidated actions

of (1) *Weissman v. United Healthcare Insurance Company, et al.*, (Civil Action 1:19-cv-10580), (2) *Cole v. United Healthcare Insurance Company*, (Civil Action 1:19-cv-12224), and (3) *Rizzuto v. United Healthcare Insurance Company, et al.* (Civil Action 1:19-cv-12239).

WHEREAS, Plaintiffs, through Class Counsel, have investigated the allegations asserted in the Litigation and have closely analyzed the merits of the alleged claims and the alleged damages suffered by the Class. Class Counsel have considered the facts, law, and potential defenses regarding the claims alleged against Defendants. Class Counsel's investigation has been adequate, and this Settlement is fully informed.

WHEREAS, after investigation, discovery, and litigation, the Parties have agreed to settle the Litigation. The Parties mediated this matter through multiple mediation sessions and extensive discussions before Edwin Oster, Esq., an experienced and well-respected private mediator with Judicate West. The Parties have conducted extensive discussions and arm's length negotiations with each other regarding the claims asserted in the Litigation.

NOW, THEREFORE, IT IS STIPULATED AND AGREED, BY AND AMONG THE PARTIES TO THIS AGREEMENT, THROUGH THEIR RESPECTIVE COUNSEL OF RECORD, AND SUBJECT TO THE APPROVAL OF THE COURT, (i) in consideration of the benefits to the Parties from the Settlement, the adequacy of which is acknowledged by the Parties, and (ii) subject to the other conditions set forth in this Agreement, that the Released Claims against the Released Parties will be finally and fully compromised, settled, and released.

DEFINITIONS

In addition to the definitions set forth elsewhere in this Agreement, the following terms used in this Agreement will have the meanings specified below.

a. "Class Counsel" means the law firms of: Arnall Golden Gregory LLP; Colson Hicks Edison; Kantor & Kantor LLP; and Kozyak, Tropin & Throckmorton LLP, and each of their

shareholders, members, partners, associates, paralegals, and employees, and their successors and assigns.

b. "Class Members" means persons who are in the *Weissman* Class.

c. "Class Representative" means each of Plaintiffs Kate Weissman, Richard Cole, and Zachary Rizzuto, and each of their respective successors and assigns.

d. "Complaint" refers to Plaintiffs' Complaints on file in this Litigation.

e. "Defendants' Counsel" means the law firm of Hogan Lovells US LLP and its partners, associates, paralegals, and employees, and its successors and assigns.

f. "Effective Date" means the first day following the date all of the following events have occurred:

i. entry of the Preliminary Approval Order;

ii. the deadline for exercising an option to terminate, as set forth in Paragraph 25, has expired, without any such option having been exercised;

iii. approval by the Court of the Settlement following class notice and a hearing and entry of Judgment; and

iv. Final Approval.

g. "Final Approval" means the expiration of the time for appeal or review of the Judgment or any part of the Judgment, including any form of further review or appeal, has been finally disposed and the time for any further appeal or review has expired. If there are no objections filed by a Class Member, Final Approval will be the date the Court grants final approval of the Settlement.

h. "Final Approval Hearing" means the final hearing held by the Court to approve this Settlement.

i. "Judgment" means the order and final judgment, in the form attached here as

Exhibit C, which provides, among other terms, for approval of the Settlement, unless the Parties agree in writing to another form of the order and final judgment.

j. The "Litigation" means the consolidated proceedings (1) *Weissman v. United Healthcare Insurance Company, et al.*, (Civil Action 1:19-cv-10580), (2) *Cole v. United Healthcare Insurance Company*, (Civil Action 1:19-cv-12224), and (3) *Rizzuto v. United Healthcare Insurance Company, et al.* (Civil Action 1:19-cv-12239) in the United States District Court for the District of Massachusetts and all claims, demands, and causes of action that were or could have been raised in either or both of those actions.

k. "Notice" means the "Notice of Proposed Settlement of Class Action and Final Approval Hearing" substantially in the form attached as **Exhibit A**.

l. "PBRT" refers to proton beam radiation therapy.

m. "Person" and "Persons" means any individual, corporation, partnership, limited liability partnership, limited liability company, association, affiliate, joint stock company, estate, trust, trustee, unincorporated association, entity, government and any political subdivision, or any other type of business or legal entity, any legal representative, and their spouses, heirs, predecessors, successors, representatives, agents, members, managers, or assignees.

n. "Preliminary Approval Order" means the Order Preliminarily Approving Settlement and Providing for Notice that the Class Representatives and United will seek from the Court, substantially in the form attached as **Exhibit B**.

o. "Related Parties" means a party's current, former, and future spouses, heirs, beneficiaries, executors, administrators, successors, predecessors, parent organizations, subsidiaries, affiliates, partners, joint venturers, officers, directors, shareholders, counsel, employees, members, managers, trustees, agents, representatives, attorneys, insurers, and assigns.

p. "Released Claims" means any and all claims, causes of action, judgments, liens, indebtedness, costs, damages, obligations, attorneys' fees, losses, claims, liabilities and demands of whatever kind or character (each "a Claim") whether representative, class, or individual in nature that are, were, or could have been asserted against any of the Released Parties by reason of or arising out of: (1) any denial made between March 26, 2016, and August 28, 2023, by United of any request (whether pre-service or post-service) for PBRT treatment for prostate cancer, primary central nervous system cancer, or cervical/gynecological cancer, for clinical reasons (including on the basis that PBRT treatment was "experimental," "investigational," or "unproven," or not medically necessary pursuant to the Medical Policy that concerns PBRT treatment) under ERISA-governed plans, either fully insured or self-insured; and/or (2) the appropriateness of United's Updated Medical Policy, attached hereto as **Exhibit D**, unless United makes future material changes to the provisions describing how coverage can be obtained for PBRT treatment for prostate cancer, primary central nervous system cancer, or cervical/gynecological cancer that restrict the availability of that coverage (which this Settlement does not restrict United's ability to do). To the extent the PBRT policy (Exhibit D), is part of a broader medical policy, this Settlement Agreement and Mutual Release applies to PBRT only. Released Claims do not include any claims for reimbursement under this Settlement, as described below, that are denied after Final Approval.

q. "Released Parties" means Defendants and their Related Parties.

r. "Settlement" means the collective settlement terms set forth in this Agreement.

s. "Settlement Administrator" means the firm that the Parties agree upon and request be appointed by the Court to disseminate notice of the pendency of the Litigation and the proposed Settlement to the Class and to otherwise administer the Settlement as set forth in this Agreement following entry of the Preliminary Approval Order and Final Approval by the Court.

t. "United Plan" refers to ERISA-governed plans issued or administered by United, including both fully insured and self-insured plans

u. "*Weissman* Class" means:

> Persons who
>
> (1) at the time they were covered by an ERISA-governed plan issued or administered by Defendants,
>
> (2) were diagnosed with one of three types of cancer at issue (prostate cancer, primary central nervous system cancer, or cervical/gynecological cancer),
>
> (3) either (a) obtained PBRT treatment and submitted a post-service claim for PBRT treatment that was denied between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data) or (b) obtained PBRT treatment after a pre-authorization denial between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data), and
>
> (4) the PBRT treatment was not paid for by any other commercial, self-funded, or governmental benefits health payor, and who do not properly exclude themselves from the Class under Paragraph 14 below.

AGREEMENT AND RELEASE

1. **Defendants' Denials of Wrongdoing and Liability.** Defendants deny each and every claim and contention alleged or otherwise made or pursued against them by Plaintiffs in the Litigation. Defendants deny all charges of wrongdoing or liability against them arising out of any of the conduct, statements, acts, or omissions that were alleged, or that could have been alleged, in the Litigation. Defendants are entering into this Settlement because they have concluded that further litigation would be protracted and expensive, and that this Settlement is desirable solely for the purpose of avoiding the burden, expense, risk, and uncertainty of continuing the proceedings.

2. **Benefits of the Settlement to the Class.** Class Representatives and Class Counsel believe that the Settlement provides fair, reasonable, and adequate recovery for the Class based on the claims asserted and the evidence developed and what might be proven by Class Representatives and the Class in the Litigation. Class Representatives and Class Counsel further recognize and acknowledge the expense and time of prosecuting the Litigation through trial and appeal. Class Representatives and Class Counsel also have considered the uncertain outcome and the risk of any litigation, including the risk that the Class might obtain no relief, especially in a complex action such as this one, as well as the difficulties and delays inherent in any complex litigation.

3. **Entry of Judgment.** If this Settlement is approved by the Court at or after the Final Approval Hearing, Class Counsel and United's Counsel will request that the Court enter the Judgment substantially in the form attached here as Exhibit C.

4. **Claims for Reimbursement**.

a. Class Members of the *Weissman* Class who paid out-of-pocket the medical costs invoiced to them by their providers for PBRT can make claims for reimbursement to the extent those payments of medical costs for PBRT have not been paid by any other commercial, self-funded, or governmental benefits health payor. A claim form substantially in the form of **Exhibit E** will be used for the submission of these claims.

b. A claim for reimbursement under this Settlement must be submitted to the Settlement Administrator within 70 days of the date the Class Notice was sent to the Class.

c. If a *Weissman* Class Member's claim for reimbursement is approved by the Settlement Administrator based on the information submitted by the Class Member, it will be subject to a cap of $75,000 for each Class Member's claim.

d. All reimbursement claims for all *Weissman* class members will be subject to an aggregate cap of $6,750,000. If this aggregate cap is met, then each class member who

submitted an approved reimbursement claim will share in the recovery on a *pro rata* basis.

5. **Release of Claims.** Each Plaintiff and each Class Member, on behalf of himself or herself and his or her Related Parties, hereby fully, finally, and forever compromises, settles, releases, resolves, relinquishes, waives, and discharges any and all Released Claims against the Released Parties. The obligations incurred under this Settlement will be the full and final disposition of the Litigation against the Released Parties.

6. **Covenant Not To Sue.** Effective immediately, each Plaintiff and Class Member agrees and covenants not to sue or prosecute, or institute or cooperate in the institution, commencement, filing, or prosecution of any suit or proceeding in any forum based upon any Released Claim against Any Released Party, except that nothing in this Agreement shall be deemed to limit any Plaintiff or Class Member's rights to enforce this Agreement.

7. **Revised Medical Policy.** United will be updating its medical policy as reflected in Exhibit D ("the Updated Medical Policy"). The Updated Medical Policy will remain in place unless United determines, based on a good faith review of the published clinical evidence and/or guidance as part of its standard medical policy review process (either as part of an annual review or another "ad hoc" or "off-cycle" review, based on new clinical evidence) that a revision is warranted in light of the current state of and/or evolving clinical evidence or guidance.

8. **Attorney's Fees and Costs.** The Parties agree that Plaintiffs can apply to the Court for, and Defendants will not oppose, payment of $2,000,000 for (i) attorneys' fees and costs, (ii) settlement administration costs, and (iii) class representative awards of $25,000 for each class representative. The Parties further agree that Plaintiffs may seek up to an additional $500,000 – for an overall request of up to (but not more than) $2,500,000 for attorneys' fees and costs, settlement administration costs, and class representative awards – and that Defendants will have the right to oppose any request by Plaintiffs that seeks more than $2,000,000 in total for (i)

attorneys' fees and costs, (ii) settlement administration costs, and (iii) class representative awards. Under no circumstance will Defendants be obligated to pay more than a combined total of $2,500,000 for (i) attorneys' fees and costs, (ii) settlement administration costs, and (iii) class representative awards. Any amounts approved by the Court for (i) attorneys' fees and costs, (ii) settlement administration costs, and (iii) class representative awards will be paid by check or wire transfer to Class Counsel within 30 days after both Final Approval and United's receipt of an IRS W-9 tax form in the name of the payee.

9. **Class Representative Awards**. Class Counsel will seek Court approval of an incentive award for Class Representatives Kate Weissman, Richard Cole, and Zachary Rizzuto in the amount of $25,000 each, based on the time and effort they devoted to the Litigation, as described in paragraph 8. United and the other Released Parties will not oppose any application for payment of any incentive award to the Class Representative, up to these amounts.

10. **Notice of Pendency and Proposed Settlement**. No more than 30 days after the entry of the Preliminary Approval Order, the Settlement Administrator will mail a notice of the proposed Settlement to each of the *Weissman* Class members. United will provide to the Settlement Administrator a list of the last known addresses and phone numbers of each person in the *Weissman* Class available from its records no later than 15 days after the entry of the Preliminary Approval Order.

a. The Settlement Administrator will send notice using the Court-approved Notice, sent by first-class mail.

b. The Settlement Administrator will perform an "NCOA" scrub on the mailing list before mailing the Mailed Notice.

c. The Settlement Administrator will perform a skip-trace search for persons whose notices are returned as undeliverable and must re-send returned mail to new addresses found

for those persons.

d. Published notice will not be required.

11. **Jurisdiction**. Each Class Member will be deemed to have submitted to the jurisdiction of the Court regarding his or her participation in the Settlement.

12. **Costs of Settlement Administration**. Plaintiffs will pay the cost of administering the settlement, including the cost of providing notice, from any award as described in paragraph 8.

13. **Jurisdiction Over Settlement Disputes**. All controversies and proceedings regarding the administration of the Settlement and distribution of attorneys' fees and costs to Class Counsel are subject to the jurisdiction of the Court.

14. **Requests for Exclusion from the Settlement Class**. Each Class Member will be bound by all determinations and judgments in the Litigation concerning the Settlement unless the member sends to the Settlement Administrator, by first class mail, a written request for exclusion from the Class. To be valid, the request for exclusion must: (1) be postmarked no later than forty-five (45) calendar days from the date the Class Notice was sent to the Class; and (2) state all of the following: (a) the name, address, and telephone number of the person requesting exclusion; and (b) a clear and unequivocal statement that the person wishes to be excluded from the Class.

15. **Effect of Exclusion**. All persons who submit valid and timely requests for exclusion in the manner described in Paragraph 14 will have no rights under this Agreement, will not share in the Settlement, and will not be bound by the Agreement or the Judgment, unless the request for exclusion is validly retracted under the terms of this Settlement Agreement and Mutual Release.

16. **List of Individuals Requesting Exclusion**. The Settlement Administrator will scan and email copies of each request for exclusion in PDF format (or any other agreed format) to

United's Counsel and to Class Counsel not more than five (5) business days after the Settlement Administrator receives such a request. As part of the motion papers in support of Final Approval of the Settlement, the Settlement Administrator or Class Counsel will provide a list of all the persons who have requested exclusion from the Class.

17. **Retraction of Exclusion Request**. Any putative Class Member may retract a prior request for exclusion by providing to Class Counsel and to United's Counsel a written notice stating his or her desire to retract the request for exclusion from the Settlement Class by 12:00 p.m., Pacific Standard Time, five (5) calendar days before the Final Approval Hearing. Any written notice retracting the request for exclusion also must include a statement that the putative Class Member makes the retraction freely and of his or her own volition, without coercion by anyone. Any putative Class Member who validly retracts a request for exclusion under this Paragraph will not be excluded from the Settlement Class, will be deemed to be a Class Member, and will be bound by the Settlement.

18. **Discretion To Nullify**. If more than five percent (5%) of Class Members submit a timely request for exclusion, United may, in its sole discretion, nullify this settlement agreement, provided that the Class Member has not validly retracted the request as of the time United exercises this option. United must declare its intent to nullify the settlement agreement no later than 30 days from the class member exclusion deadline. If United exercises this option, United will be responsible for the payment of 50% of the settlement administration costs incurred through the date on which it declared its intent to nullify the settlement agreement. In all other respects, the Settlement and this Agreement will become null and void and have no further force and effect.

19. **Objections To Settlement**. Any Class Member who wishes to object to the fairness, reasonableness, or adequacy of this Agreement or the proposed Settlement must deliver to Class Counsel and to United's Counsel, no later than forty-five (45) calendar days from the date

Mailed Notice was sent to the Class Members or as the Court otherwise may direct, a written statement of the objections, as well as the specific reason(s), if any, for each objection, including any legal support the Class Member wishes to bring to the Court's attention and any evidence or other information the Class Member wishes to introduce in support of the objections. Class Members may object either on their own or through an attorney retained at their own expense. The written objection must also contain the Class Member's name, address, signature, and telephone number.

20. **Appearance at Final Approval Hearing**. Any Class Member who files and serves a written objection, as described in Paragraph 19, may appear at the Final Approval Hearing, either in person or through counsel hired at the Class Member's expense, to object to the fairness, reasonableness, or adequacy of this Agreement or the proposed Settlement. Class Members or their attorneys who intend to make an appearance at the Final Approval Hearing must deliver a notice of intention to appear to Class Counsel and to United's Counsel, and file that notice with the Court, no later than forty-five (45) calendar days from the date Notice was sent to the Class Members as the Court may otherwise direct.

21. **Forfeiture of Right to Object**. Any Class Member who fails to comply with the provisions of this Section will waive and forfeit any and all rights he or she may have to appear separately and object, and will be bound by all the terms of this Agreement and by all proceedings, orders, and judgments, including but not limited to the Release, in the Litigation.

22. **Objecting Class Member's Entitlement to Benefits Upon Approval**. Any Class Member who objects to the Settlement will be entitled to all of the benefits of the Settlement if it is approved, as long as the objecting Class Member complies with all requirements of this Agreement.

23. **Preliminary Approval Order**. Class Counsel will promptly file the Agreement

and its exhibits with the Court and apply for entry of the Preliminary Approval Order substantially in the form attached here as Exhibit B.

24. **Settlement Process Schedule**. The dates for the events contemplated by this Settlement Agreement are as follows:

Event Date	**Event**
15 days from the date of the Preliminary Approval Order	United provides data for Class Members to the Settlement Administrator
30 days from the date of the Preliminary Approval Order	The Administrator mails and/or emails the notice of the proposed Settlement
35 days from the date of the Preliminary Approval Order	Class Counsel files a motion for an award of attorneys' fees and costs and class representative incentive award
75 days from the date of the Preliminary Approval Order	Deadline for postmarking of exclusions, objections, and requests to be heard at the Final Approval Hearing
80 days from the date of the Preliminary Approval Order	Class Counsel to file notice specifying those who have objected, together with a declaration of the Settlement Administrator
100 days from the date of the Preliminary Approval Order	Deadline for class members to submit a claim for reimbursement under this Settlement
21 days prior to the Final Approval Hearing	Class Counsel to file a motion for final approval
To be set by the Court, at least 130 days after the date of the Preliminary Approval Order	Final Approval Hearing

25. **Termination of the Settlement**. Either Party will have the option to terminate this Agreement on ten (10) calendar days' notice to the other if any of the following occurs:

a. The Court enters any order that is materially inconsistent with the terms of this Agreement;

b. The Court does not enter the Preliminary Approval Order;

c. The Court does not approve the Settlement or any material part of it as reflected in this Agreement (although the Parties do not concede that every term of the Settlement or of this Agreement is material for these purposes);

d. The Court does not enter the Judgment; or

e. The Judgment is vacated, modified, or reversed in any material respect by an appellate court of competent jurisdiction.

26. **Effect of Termination**. If this Agreement is terminated, the Settlement and this Agreement will become null and void and will have no further force and effect. If this Agreement is terminated, the Parties to this Agreement will be deemed to have reverted *nunc pro tunc* to their respective status in the Litigation as of the date and time immediately before the execution of this Agreement. Except as otherwise expressly provided, the Parties will proceed in all respects as if this Agreement and any related orders had not been entered and without any prejudice in any way from the negotiation, fact, or terms of the Settlement or this Agreement.

27. **No Other Use of Settlement Agreement**. This Agreement may not be used in the Litigation or in any other proceeding for any purpose, and any Judgment or order entered by the Court in accordance with the terms of this Agreement, except as provided in paragraph 3, will be treated as vacated, *nunc pro tunc*.

28. **No Admission of Wrongdoing or Liability**. Whether or not the Settlement is approved by the Court, and whether or not it is consummated, the fact and terms of this Agreement, including Exhibits, all negotiations, discussions, drafts, and proceedings in connection with the Settlement, and any act performed or document signed in connection with the Settlement:

a. may not be construed, offered, or received against United or any other Released Party as a presumption, concession, or admission about the truth of any fact alleged by Plaintiffs, the validity of any claim that had been or could have been asserted in the Litigation or

in any litigation, that the class should have been certified, or the deficiency of any defense that has been or could have been asserted in the Litigation or in any litigation; and

b. may not be construed, offered, or received against Plaintiffs or the Class or any of them as a presumption, concession, or admission that any of their claims are or were without merit or that any damages recoverable under the Complaint would not have exceeded any benefits provided under this Settlement.

29. **Settlement As Defense in Future Action**. Once approved by the Court, the Settlement reflected in this Agreement may be pleaded as a full and complete defense by any of the Released Parties to any action, suit, or other proceeding that may be instituted, prosecuted, or attempted regarding any of the Released Claims. The Released Parties may offer the Agreement or the Judgment from the Litigation in any other action that may be brought against them by any identified Class Member in order to support a defense or counterclaim based on principles of *res judicata*, collateral estoppel, release, good faith settlement, judgment bar or reduction, or any similar defense or counterclaim.

30. **Agreement To Work in Good Faith**. The Parties agree to work together in good faith to accomplish, as soon as reasonably practical, all of the prerequisites for the Effective Date, including the Preliminary Approval Order, approval by the Court of the Settlement, and the Judgment.

31. **Headings.** The headings and paragraph titles in this Agreement are used for the purpose of convenience only and are not meant to have legal effect.

32. **Incorporation of Exhibits**. All of the Exhibits attached to the Agreement are incorporated by reference. If there is a conflict or inconsistency between the terms of this Agreement and the terms of any exhibit, the terms of this Agreement will prevail.

33. **Amendments in Writing Only.** This Agreement may not be modified or amended, nor may any of its provisions be waived, except by a writing signed by all Parties or their successors-in-interest.

34. **Full and Final Settlement**. The Parties to this Agreement intend the Settlement to be a final and complete resolution of all disputes asserted or which could be asserted by Plaintiffs and the Class Members against any of the Released Parties with respect to the Released Claims.

35. **Arm's Length and Good Faith Agreement**. The Parties to this Agreement agree that the terms of the Settlement were negotiated at arm's length in good faith by the Parties and reflect a settlement that was reached voluntarily based on adequate information and after consultation with experienced legal counsel.

36. **Waiver**. The waiver by one Party of any breach of this Agreement by any other Party will not be deemed a waiver of any other prior or subsequent breach of this Agreement.

37. **Entire Agreement**. This Agreement and its Exhibits constitute the entire agreement among the Parties regarding the Settlement and supersede all prior and contemporaneous arrangements, oral and written agreements, and discussions or negotiations between or among the Parties or their agents or attorneys. No promise, representation, or warranty by any Party, or attorney or agent of any Party, regarding the Settlement that is not expressly contained or referred to in this Agreement or its exhibits will be valid or binding on that Party. The Parties have included this Paragraph to preclude the introduction of parole evidence to vary, supplement, or contradict the terms of this Agreement.

38. **Signature in Counterparts**. This Agreement may be executed by electronic signature (as indicated by an "s/"), and in one or more counterparts, including by signature transmitted by facsimile, or by a .pdf/.tiff image of the signature transmitted by email. All executed counterparts and each of them will be deemed to be one and the same instrument.

39. **Best Efforts**. The Parties and their respective counsel agree that they will use their best efforts to obtain all necessary approvals of the Court required for the Settlement by this Agreement.

40. **Necessary Authority**. Each person signing this Agreement represents that he or she has all necessary authority to sign this Agreement and bind the Party on whose behalf he or she signs.

41. **Non-Assignment**. This Agreement will be binding on the Parties, including any and all Released Parties and any corporation, partnership, or other entity into or with which any Party may merge, consolidate, or reorganize. No assignment will relieve any Party of any obligation under this Settlement.

42. **Notice**. Notices required by this Agreement will be submitted both (1) by email and (2) either by (a) any form of overnight mail or (b) in person to:

Stephanie A. Casey
COLSON HICKS EIDSON P.A.
255 Alhambra Circle, Penthouse
Coral Gables, FL 33134

Maria Dolores Garcia
Robert J. Neary
KOZYAK TROPIN & THROCKMORTON LLP
2525 Ponce de Leon Blvd., 9th Floor
Coral Gables, FL 33134

Richard T. Collins
ARNALL GOLDEN GREGORY LLP
2100 Pennsylvania Avenue, NW, Suite 350S
Washington, DC 20037

Lisa Kantor
Tim Rozelle
KANTOR & KANTOR, LLP
9301 Corbin Ave., Suite 1400
Northridge, CA 91324

Attorneys for Plaintiffs

and

Peter Walsh
HOGAN LOVELLS US LLP
80 South 8th Street, Suite 1225
Minneapolis, MN 55402

Michael M. Maddigan
HOGAN LOVELLS US LLP
1999 Avenue of the Stars, Suite 1400
Los Angeles, CA 90067
Attorneys for Defendants

Notice will be deemed effective on sending the notice as described in this Paragraph.

43. **Retention of Jurisdiction**. The administration, consummation, and enforcement of the Settlement in this Agreement will be under the authority of the Court, and the Parties intend that the Court retain jurisdiction for the purpose of entering orders, providing for approval of attorneys' fees and costs to Class Counsel, and enforcing the terms of the Settlement and this Agreement.

44. **Massachusetts Law**. The construction, interpretation, operation, effect, and validity of this Agreement, and all documents necessary to effectuate it, will be governed by the internal laws of the Commonwealth of Massachusetts without regard to conflicts of laws.

45. **No Interpretation Against Drafter**. This Agreement will not be construed more strictly against one Party than another merely by virtue of the fact that it, or any part of it, may have been prepared by counsel for one of the Parties. This Agreement is the result of arm's length negotiations between the Parties and all Parties have contributed substantially and materially to the preparation of this Agreement.

IN WITNESS WHEREOF the parties hereto have executed this Agreement on the dates written below.

ACCEPTED AND AGREED:

DEFENDANTS UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICES, LLC

Dated: _____

By: _____
Name:
Their:

DEFENDANT INTERRPUBLIC GROUP OF COMPANIES, INC., CHOICE PLUS PLAN

By: _____
Name:
Their:

THE HERTZ CUSTOM BENEFIT PROGRAM

By: _____
Name:
Their:

PLAINTIFF KATE WEISSMAN

Dated: _____ _____

PLAINTIFF RICHARD COLE

Dated: 5/8/2025

DocuSigned by:
Richard Cole
41FD845C4FF545D...

PLAINTIFF ZACHARY RIZUTTO

Dated: _____ _____

APPROVED AS TO FORM:

HOGAN LOVELLS US LLP

Dated: _____ _____
Michael M. Maddigan
Counsel for Defendants

Dated: 5/9/2025 _____
Robert J. Neary
Counsel for Plaintiffs and on behalf of all Plaintiffs' Counsel

IN WITNESS WHEREOF the parties hereto have executed this Agreement on the dates written below.

ACCEPTED AND AGREED:

DEFENDANTS UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICES, LLC

Dated: 5/9/25

By: _____
Name: Steven Bursten
Their: Deputy General Counsel

DEFENDANT INTERRPUBLIC GROUP OF COMPANIES, INC., CHOICE PLUS PLAN

By: _____
Name:
Their:

THE HERTZ CUSTOM BENEFIT PROGRAM

By: _____
Name:
Their:

PLAINTIFF KATE WEISSMAN

Dated: _____ _____

PLAINTIFF RICHARD COLE

Dated: _____ _____

PLAINTIFF ZACHARY RIZUTTO

Dated: _____ _____

APPROVED AS TO FORM:

HOGAN LOVELLS US LLP

Dated: 5/9/25 _____

Michael M. Maddigan
Counsel for Defendants

_____

Dated: _____

Robert J. Neary
Counsel for Plaintiffs and on behalf of all Plaintiffs' Counsel

IN WITNESS WHEREOF the parties hereto have executed this Agreement on the dates written below.

ACCEPTED AND AGREED:

DEFENDANTS UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICES, LLC

Dated: 5/8/2025

By: _____
Name:
Their:

DEFENDANT INTERRPUBLIC GROUP OF COMPANIES, INC., CHOICE PLUS PLAN

By: _____
Name:
Their:

THE HERTZ CUSTOM BENEFIT PROGRAM

By: _____
Name: Randall J. White
Their: VP, Chief Counsel

PLAINTIFF KATE WEISSMAN

Dated: _____ _____

PLAINTIFF RICHARD COLE

Dated: _____ _____

IN WITNESS WHEREOF the parties hereto have executed this Agreement on the dates written below.

ACCEPTED AND AGREED:

DEFENDANTS UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICES, LLC

Dated: _____

By: _____
Name:
Their:

DEFENDANT INTERRPUBLIC GROUP OF COMPANIES, INC., CHOICE PLUS PLAN

By: Ileana H. Kutler
Name: Ileana H. Kutler
Their: SVP, Associate General Counsel

THE HERTZ CUSTOM BENEFIT PROGRAM

By: _____
Name:
Their:

PLAINTIFF KATE WEISSMAN

Dated: _____ _____

PLAINTIFF RICHARD COLE

Dated: _____ _____

IN WITNESS WHEREOF the parties hereto have executed this Agreement on the dates written below.

ACCEPTED AND AGREED:

DEFENDANTS UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICES, LLC

Dated: _____

By: _____
Name:
Their:

DEFENDANT INTERRPUBLIC GROUP OF COMPANIES, INC., CHOICE PLUS PLAN

By: _____
Name:
Their:

THE HERTZ CUSTOM BENEFIT PROGRAM

By: _____
Name:
Their:

PLAINTIFF KATE WEISSMAN

Dated: 5/9/2025

DocuSigned by:
Kate Weissman
2F621DCF8D8E4DE...

PLAINTIFF RICHARD COLE

Dated: _____

_____

PLAINTIFF ZACHARY RIZUTTO

Dated: 5/9/2025

Signed by:
370B1205EB8E421...

APPROVED AS TO FORM:

HOGAN LOVELLS US LLP

Dated: _____

Michael M. Maddigan
Counsel for Defendants

Dated: _____

[Name]
Counsel for Plaintiffs

EXHIBIT A

NOTICE OF PROPOSED CLASS ACTION SETTLEMENT

PLEASE DO NOT DISCARD THIS NOTICE AND READ IT CAREFULLY
THIS SETTLEMENT AFFECTS YOUR LEGAL RIGHTS

You have received this Notice because records indicate that you were a member, participant, and/or beneficiary of an employee welfare benefit plan governed by the Employee Retirement Income Security Act of 1974 ("ERISA"), which was administered and/or insured by UnitedHealthcare Insurance Company and/or UnitedHealthcare Services, LLC (together "UnitedHealthcare"). In addition, between March 26, 2016, and August 28, 2023, you for yourself, or a beneficiary covered by your benefit plan, received a denial of a precertification request or post-service benefit claim and may have paid out-of-pocket for proton beam radiation therapy ("PBRT") to treat one of the following three types of cancer: prostate cancer; central nervous system cancer; or cervical/gynecological cancer.

This Settlement makes available up to $6.75 million to be used to pay up to $75,000 per claim as reimbursement for you paying for PBRT for the treatment of any of three cancers noted above.

This Notice contains summary information with respect to the Settlement. The complete terms and conditions of the Settlement are set forth in the Settlement Agreement ("Settlement Agreement"). Capitalized terms used in this Notice, but not defined in this Notice, have the meanings assigned to them in the Settlement Agreement. The Settlement Agreement, and additional information with respect to this lawsuit and the Settlement is available at the website dedicated to the Settlement, www._____.com.

The United States District Court for the District of Massachusetts authorized this Notice. This is not a solicitation from a lawyer. The Court in charge of this case is the United States District Court for Massachusetts, and the case is titled Kate Weissman v. UnitedHealthcare Insurance Company, et al, Case No. 1:19-cv-10580 (the "Action").

YOUR LEGAL RIGHTS AND OPTIONS IN THIS SETTLEMENT	
SUBMIT A CLAIM FORM	**Submitting a Settlement Claim Form is the only way to get a payment in this Settlement.** The Settlement Claim Form is enclosed with this Notice. UnitedHealthcare's records indicate that you may qualify as a Settlement Class Member. By submitting the enclosed Claim Form you can establish your membership in the Class. **All Settlement Class Members who complete and timely submit the enclosed Settlement Claim Form establishing their membership in the Class can receive a payment of up to $75,000**, with the submission of proof of payment for PBRT treatment.
DO NOTHING	If you do not submit a Settlement Claim Form and take no further action, you will not receive any payment and you will still be bound by the terms of the Settlement.
EXCLUDE YOURSELF	You will not receive any payment. This is the only option that allows you to ever be a part of any other lawsuit against UnitedHealthcare, Interpublic Group of Companies, Inc., Choice Plus Plan, the Hertz Custom Benefit Program, or other "Related Parties" related to the legal claims at issue in this case.

OBJECT TO THE SETTLEMENT	Advise the Court of your disagreement with the Settlement.
GO TO A HEARING	Ask to speak in Court about the fairness of the Settlement, at a hearing that the Court has scheduled for _____, 2025.

- These rights and options, and the deadlines to exercise them, are explained in this Notice.
- The Court still has to decide whether to approve the Settlement. Payments will be made only if the Court approves the Settlement and it is held up in the event of an appeal.

WHAT THIS NOTICE CONTAINS

BASIC INFORMATION

1. Why did I get this Letter?

You are receiving this letter (called a "Notice") and the enclosed Settlement Claim Form because the Parties believe that you may be a Settlement Class Member, based on a review of UnitedHealthcare's records.

The Court authorized this Notice and enclosed Settlement Claim Form because you have a right to know about a proposed settlement of this class action, and about all of your options, before the Court decides whether to give "final approval" to the Settlement. If the Court approves the Parties' Class Action Settlement Agreement ("Settlement Agreement"), and after any objections and appeals are resolved, payments will be made to those who qualify.

This Notice explains the Action, the Settlement, your legal rights, what benefits are available under the Settlement, who is eligible for them, and how to receive them.

The individuals who filed this Action, Kate Weissman, Richard Cole, and Zachary Rizzuto, are called the Plaintiffs, and the companies they sued, UnitedHealthcare Insurance Company, UnitedHealthcare Services, LLC, Interpublic Group of Companies, Inc., Choice Plus Plan, and the Hertz Custom Benefit Program, are called the "Defendants" in this Notice.

2. Which companies are part of the Settlement?

This Settlement involves Defendants UnitedHealthcare Insurance Company, UnitedHealthcare Services, LLC, Interpublic Group of Companies, Inc., Choice Plus Plan, and the Hertz Custom Benefit Program.

3. What is this Action about?

Plaintiffs Kate Weissman, Richard Cole, and Zachary Rizzuto, on their own behalf and on behalf of other persons similarly situated, filed the Action against Defendants alleging generally that during a period of several years, Defendants wrongfully denied precertification requests and post benefit claims for PBRT.

Defendants deny that they did anything wrong, and maintain that they complied with their obligations under the respective ERISA-governed employee welfare benefit plans and with all applicable laws. However, the Parties have agreed to settle the Action to avoid the cost, delay, and uncertainty of continued litigation.

4. Why is this a class action?

In a class action lawsuit, one or more people called "Class Representatives" (in this case, Kate Weissman, Richard Cole, and Zachary Rizzuto) sued on behalf of a group of people who have similar claims. All of these people together are a "Class" or "Settlement Class Members." One court resolves the issues of all Settlement Class Members, except for those people who choose to exclude themselves from the Class. Judge Allison D. Burroughs of the United States District Court for the District of Massachusetts is the federal judge presiding over this class action.

5. Why is there a settlement?

After this matter was filed, but before it reached trial, both sides agreed to a Settlement, which, if approved, brings the Action to an end. That way, Plaintiffs and Defendants avoid the cost, delay, and uncertainty of moving forward in litigation to trial and possible appeals, and the Settlement Class Members are eligible for payments. The Class Representatives and their attorneys think that settlement is best for the Settlement Class Members and that the Settlement is fair, adequate, and reasonable.

WHO IS IN THE SETTLEMENT

6. How do I know if I am part of the Class and Settlement?

Based on a review of UnitedHealthcare's records, you are receiving this Notice because the Parties believe that you may be a member of the Class, and therefore part of the Settlement.

The Class includes all members, participants, and beneficiaries of ERISA-governed employee welfare benefit plans administered and/or insured by UnitedHealthcare, who:

- were diagnosed with either prostate cancer; primary central nervous system cancer, or cervical/gynecological cancer; AND
- either (a) obtained PBRT treatment and submitted a post-service claim for PBRT treatment that was denied between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data) or (b) obtained PBRT treatment after a pre-authorization denial between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data); AND
- the PBRT treatment was not paid for by any other commercial, self-funded, or governmental health benefits payor.

If you were sent this Notice by the Claims Administrator and your name and your current or previous address appears as the intended recipient of the Notice, that means that UnitedHealthcare's records indicate you may be a Settlement Class Member.

See Question 7 below for exceptions to the Class definition.

7. Are there exceptions to being included in the Class?

Yes. Excluded from the Class are: (1) individuals who received coverage for PBRT from another commercial, self-funded, or governmental health benefits payor; and/or (2) Defendants, as well as Defendants' affiliates, attorneys, agents, insurers, the attorneys representing Defendants in this case; and (3) the Judge to whom this case is assigned and their immediate family members and staff.

8. I'm still not sure if I am included.

If you are still not sure whether you are included, you can get free help. You can send an e-mail to mail@_____.com; or visit www. _____.com for more information.

THE SETTLEMENT BENEFITS

9. What does the Settlement provide?

Provided that the Settlement becomes final, Settlement Class Members who timely submit a valid Claim along with proof of payment or proof of what you owe (see Question 11 below), may be entitled to a payment of up to $75,000 as outlined below. In addition to the cash payment, UnitedHealthcare has agreed to revise its PBRT policy which Plaintiffs' counsel believe will make it easier for patients to have their PBRT coverage requests properly reviewed for approval. Among other things, the revised PBRT medical policy recognizes that PBRT is proven and considered clinically equivalent to traditional radiation for treating prostate cancer; allows a patient to obtain PBRT treatment when the patient provides certain documentation demonstrating that sparing of the surrounding normal tissue cannot be achieved with standard radiation therapy techniques; and the policy no longer includes specific references to a list of thirteen diagnoses or uses for which, proton beam therapy was deemed "unproven and not medically necessary."

In return, Settlement Class Members will be providing Defendants with a release of claims as outlined below (see Question 16).

The above description is just a summary. The complete terms of the payments, changes to United's PBRT policy, and the Released Claims can be found in the Settlement Agreement.

10. What do I need to do to participate in the Settlement and how much could my payment be?

Each Settlement Class Member who completes and timely submits the enclosed Settlement Claim Form establishing their membership in the Class and providing their proof of payment or proof of what they owe can receive a payment of up to **$75,000**. However, in the event that the amount of claim form submissions by Settlement Class Members total more than $6,750,000.00 then each class member who submitted an approved reimbursement claim will share in the recovery on a *pro rata* basis.

A**ppropriate proof of payment must be submitted as described in Question 11, below**.

If you decide to submit a completed Settlement Claim Form and appropriate proof, if applicable, you must send these materials to the Claims Administrator via e-mail to _____, by First Class Mail to _____, or by uploading the documents and claim form to www._____.com. The claim form and documents must be emailed, uploaded, or mailed and post-marked, by _____.

Your final payment will be calculated and then distributed according to the process described in Question 10.

11. What is the appropriate proof that needs to be submitted to receive a payment of up to $75,000?

If you are seeking reimbursement for your payment for PBRT treatment, **you must also submit with your Settlement Claim Form proof of payment and/or proof of any additional amounts you still owe for PBRT treatment,** to verify that you paid an amount and/or incurred debt for PBRT treatment for the three cancer types that are part of this Settlement.

- **Proof of payment** includes, but is not limited to, receipt(s) showing payment for Proton Beam Therapy treatment from a hospital, treatment center, or physician; cancelled checks; credit card records; or any other proof of payment for Proton Beam Therapy treatment, including documentation from UnitedHealthcare Insurance Co.

- **Proof of what you owe** includes, but is not limited to, loan documentation; current collection notices; unpaid and currently owing invoices or bills from the medical provider or facility; or existing self-pay agreements with a medical care provider that administered Proton Beam Therapy treatment.

Accordingly, Defendants will be making available up to the amount of $6,750,000. Should the amount of claim form submissions by Settlement Class Members total more than $6,750,000 then each class member who submitted an approved reimbursement claim will share in the recovery on a *pro rata* basis.

If the Settlement becomes final, the Action will be dismissed with prejudice (*i.e.*, cannot be brought against Defendants again), and Defendants and others will receive a complete release and discharge of the claims asserted in the Action from Plaintiffs and every Settlement Class Member. (See Questions 16 and 25 through 28 for more details.)

12. Who is the Claims Administrator?

The Claims Administrator is Rust Consulting, Inc. You can call the Claims Administrator toll-free at 1-___-_____; send an e-mail to _____@_____.com; or visit www. _____.com for more information. The Claims Administrator's mailing address can be found in Question 13.

13. If I am the intended recipient of this Notice, but my address has changed, what do I do to let you know my new address so that the check is sent to me at the right place?

For your convenience, there is a Change of Address Form at the end of this Notice. You must fill it out completely (providing your current address) and send the Form via First Class Mail so that it is **post-marked by** _____ to the following address:

P.O. Box _____

_____,__ _____

If you are a Settlement Class Member's Legally Authorized Representative (see Question 17), and your address has changed, you must also fill out the second page of the Address Verification Form and provide your own contact and other information.

You also may complete the Change of Address Form on the Settlement website, www._____.com. The deadline for doing so is _____.

14. When will I get my payment?

The exact date that qualifying Settlement Class Members will receive payment is not known at this time, because it depends on events as described below.

The Court must first hold a hearing on **_____ __, ____, at ____ a.m. (Eastern time)** to decide whether to finally approve the Settlement. If the Court approves the Settlement (see Question 25 below), there may be appeals. It is always uncertain whether these appeals can be resolved, and resolving them could take time.

If the Court approves the Settlement, and the Settlement becomes final, the Claims Administrator will begin sending payments to Settlement Class Members (within a reasonable period) after the Settlement becomes final.

The Settlement website (www. _____.com) will post important scheduling updates. You can always call us toll-free at 1-___-___-____ or send an e-mail to _____@_____.com to learn the status. You may also contact Class Counsel (see Question 21 for contact information).

15. What if I disagree with the amount of my payment?

If you submit a Settlement Claim that is denied in whole or in part, the Claims Administrator will send you a written explanation of the denial by First Class Mail. The denial notice will also inform you that you have a right to appeal if you disagree with the Claims Administrator's decision. **You will have thirty days in which to send the Claims Administrator a written appeal that explains why you disagree with the decision, which you must send by e-mail or First-Class Mail to the Claims Administrator.** The Claims Administrator will provide copies to Class Counsel and Defendants' Counsel who will then review your appeal and meet to discuss whether your appeal should be granted. In the event the Parties' counsel cannot agree, they will submit the appeal to the Court for entry of a final, binding, and non-appealable ruling.

16. What am I giving up to get a payment?

Unless you exclude yourself, you will remain in the Class, and that means that you can't be part of any other lawsuit against Defendants or any "Related Parties" (as that term is defined in the Settlement Agreement) about the legal issues in ***this*** case. It also means that all of the Court's orders will apply to you and legally bind you. If you remain in the Class, you will agree to release Defendants and the Related Parties from claims as described in Paragraph 5 of the Settlement Agreement.

A complete copy of the Settlement Agreement can be obtained at www. _____.com. The Settlement Agreement specifically describes the Released Claims in necessarily accurate legal terminology. You may contact Class Counsel (see Question 21) or your own lawyer if you have questions about the Released Claims or what they mean. Please note that you are free to hire your own lawyer with respect to the Settlement at your own expense, which is not reimbursable through Defendants or otherwise.

EXCLUDING YOURSELF FROM THE SETTLEMENT

If you don't want a payment from this Settlement, but you want to keep the right to sue Defendants on your own about the legal issues in this case, then you must take steps to exclude yourself from this Settlement. Excluding yourself from this Settlement is sometimes referred to as "opting out" of the Class.

17. How do I exclude myself from the Settlement?

If you exclude yourself from the Class by "opting out" you won't get any money from this Settlement. However, you will retain any right you currently have to make your own claim against the Defendants.

To exclude yourself from the Settlement, you must send a letter to the Claims Administrator by First Class Mail with a clear and unequivocal statement that you want to be excluded from the *Weissman v. UnitedHealthcare Ins. Co., et al.* settlement.

To be valid the exclusion request must include your name, address, telephone number, and your signature. If you are sending the request to be excluded as the Legally Authorized Representative of a Settlement Class Member (see Question 18 for the definition of that term), you must include any information or documents that confirm your appointment or status as a Legally Authorized Representative. Requests for exclusion must be submitted individually by a Settlement Class Member or his or her Legally Authorized Representative, and not on behalf of a group or class of persons. If you have a personal lawyer, your lawyer may assist you with your exclusion request, but you must sign the exclusion request, unless the lawyer is also your Legally Authorized Representative.

You must mail your exclusion request **post-marked no later than _____,** to:

P.O. Box _____
_____,__ _____

18. What is a "Legally Authorized Representative"?

"Legally Authorized Representative" means an administrator/administratrix or executor/executrix of the estate of a deceased Settlement Class Member, a guardian or conservator of an incapacitated Settlement Class Member or any other legally appointed person or entity having legal power of attorney for the business affairs of a Settlement Class Member. A Legally Authorized Representative does not include a professional objector or claim filing or similar service purporting to act on behalf of an individual Settlement Class Member or group of Settlement Class Members.

19. If I don't exclude myself, can I sue the Defendants for the same thing later?

No. Unless you exclude yourself, you give up any right to sue the Defendants or the Related Parties for the claims at issue in this Action. If you have a pending lawsuit or dispute against UnitedHealthcare or the other Defendants, speak to your lawyer in that case immediately. If you do have a pending lawsuit or dispute against UnitedHealthcare that involves claims being released through this Settlement, you must exclude yourself from ***this*** Class to continue your own pending lawsuit. **Remember, the exclusion deadline is _____, 20__.**

20. If I exclude myself, can I get a payment from this Settlement?

No. If you exclude yourself, you are not eligible for a payment under the Settlement.

THE LAWYERS REPRESENTING YOU

21. Do I have a lawyer in this case?

The Court has approved the following lawyers and their respective law firms as Class Counsel to represent you and the other Settlement Class Members if you do not choose to exclude yourself from the Settlement:

Richard T. Collins
Landen Benson
ARNALL GOLDEN GREGORY LLP
2100 Pennsylvania Avenue, NW, Suite 350S
Washington, DC 20037
Tel: (202) 677-4917
Email:
Rich.Collins@AGG. com
Landen.Benson@AGG.com

Lisa Kantor
Tim Rozelle
KANTOR & KANTOR LLP
9301 Corbin Ave., Suite 1400
Northridge, CA 91324
Tel: (866) 783-1036
Email:
Lkantor@kantorlaw.net
Trozelle@kantorlaw.net

Stephanie A. Casey
COLSON HICKS EIDSON, P.A.
255 Alhambra Circle, Penthouse
Coral Gables, Florida 33134
Tel.: (305) 476-7400
Email: scasey@colson.com

Maria D. Garcia
Robert J. Neary
KOZYAK TROPIN & THROCKMORTON, LLP
2525 Ponce de Leon, 9th Floor
Coral Gables, Florida 33134
Tel.: (305) 372-1800
Email:
mgarcia@kttlaw.com

rn@kttlaw.com

22. How will the lawyers be paid?

Class Counsels' fees and costs will be determined by the Court and will be paid by Defendants separate and apart from your individual recovery. You will not be charged for Class Counsels' work in securing the Settlement benefits for you and the other Settlement Class Members. You owe nothing if you participate in the Settlement. If you want to be represented by your own lawyer, you may hire one at your own expense.

Class Counsel will ask the Court for an award of attorneys' fees and expenses that does not exceed $2,500,000. This amount includes attorneys' fees, litigation expenses, the costs incurred by the Claims Administrator, and service awards to the Class Representatives. The Court may award and allow payment of less than this amount. Any award of attorneys' fees and expenses will ***not*** impact or reduce any payments issued to the Settlement Class Members. Defendants have agreed not to oppose the request for Class Counsel's reasonable fees and expenses up to $2,000,000. Defendants have the right to oppose the additional $500,000 sought by Class Counsel

OBJECTING TO THE SETTLEMENT

If you are a Settlement Class Member and do not exclude yourself, you can tell the Court that you don't agree with the Settlement or some part of it.

23. How do I tell the Court that I object to the Settlement?

If you're a Settlement Class Member (or a Settlement Class Member's Legally Authorized Representative, see Question 18), and you haven't excluded yourself from the Settlement, you can—but don't have to—object to the Settlement. You can give reasons why you think the Court should not approve any aspect of it. The Court will consider your views.

For the Court to consider a notice of intent to object to the Settlement, it must: (a) contain a heading which includes the name of the case (*Weissman v. UnitedHealthcare Ins. Co., et al*); (b) provide the Settlement Class Member's full name, address, telephone number, and signature; (c) be delivered to Class Counsel and Defendants' Counsel at the addresses below, post-marked no later than _____; (d) contain the name, address, bar number and telephone number of the objecting Settlement Class Member's counsel, if represented by an attorney; (e) contain a detailed statement of the position(s) the objector wishes to assert, including the factual and legal grounds for the position(s); and (h) include any documents that the objector wishes to submit in support of his/her position(s).

Address of Class Counsel:

Richard T. Collins
ARNALL GOLDEN GREGORY LLP
2100 Pennsylvania Avenue, NW, Suite 350S
Washington, DC 20037

Lisa Kantor

Address of Defendants' Counsel:

Peter Walsh, Esq.
HOGAN LOVELLS US LLP
80 South 8th Street, Suite 1225
Minneapolis, MN 55402

Tim Rozelle
KANTOR & KANTOR LLP
9301 Corbin Ave., Suite 1400
Northridge, CA 91324

Stephanie A. Casey, Esq.
COLSON HICKS EIDSON, P.A.
255 Alhambra Circle, Penthouse
Coral Gables, Florida 33134

Maria D. Garcia, Esq.
Robert J. Neary, Esq.
KOZYAK TROPIN &
THROCKMORTON, LLP
2525 Ponce de Leon, 9th Floor
Coral Gables, Florida 33134

Attorneys for the Plaintiffs and the Settlement Class

Michael M. Maddigan, Esq.
HOGAN LOVELLS US LLP
1999 Avenue of the Stars, Suite 1400
Los Angeles, CA 90067

Attorneys for Defendants

Any comments or objections, which do not comply with the above or are not timely served on all counsel listed above will not be considered by the Court.

24. What's the difference between objecting and excluding yourself?

Objecting is simply telling the Court that you don't like something about the Settlement. You can object only if you stay in the Class. Excluding yourself is telling the Court that you don't want to be part of the Class. If you object, and the Court approves the Settlement anyway, you will still be legally bound by the result. If you exclude yourself, you have no basis to object, because the case no longer affects you.

THE COURT'S FINAL APPROVAL HEARING

The Court will hold a hearing called a "Final Approval Hearing" (also known as a "Fairness Hearing") to decide whether to approve the Settlement.

25. When and where will the Court decide whether to approve the Settlement?

The Court will hold a Final Approval Hearing to decide whether to finally approve the proposed Settlement.

The Final Approval Hearing will be on **_____, at _____ a.m. (Eastern time)** before Judge Allison D. Burroughs, United States District Court for the District of Massachusetts, John Joseph Moakley U.S. Courthouse, 1 Courthouse Way, Suite 2300, Courtroom #17 (5th floor), Boston, Massachusetts 02210.

At this Hearing, the Court will consider whether the proposed Settlement and all of its terms are adequate, fair, and reasonable. If there are valid objections, the Court will consider them. The Court may listen to Settlement

Class Members (or their individual attorneys) who have asked for permission to speak at the Hearing and complied with the other requirements for objections explained in Question 23 above. The Court may also decide how much to award Class Counsel for fees and expenses for representing the Class.

At or after the Hearing, the Court will decide whether to finally approve the proposed Settlement. There may be appeals after that. We do not know how long these decisions will take.

The Court may change deadlines listed in this Notice without further notice to the Class. To keep up on any changes in the deadlines, please contact the Claims Administrator or review the website.

26. Do I have to come to the Hearing?

No. Class Counsel will answer any questions asked by the Court, but you are welcome to come at your own expense. If you intend to have a lawyer appear at your expense and speak to the Court on your behalf at the Final Approval Hearing, your lawyer must enter a written notice of appearance of counsel with the Clerk of Court no later than **_____,** and you must comply with all of the requirements explained in Question 27.

If you send an objection, you don't have to come to Court to talk about it. So long as you submitted your written objection on time and complied with the other requirements for a proper objection, the Court will consider it.

27. May I speak at the Hearing?

You may attend and you may ask the Court to speak, but you don't have to do either one.

If you submitted a proper written objection to the Settlement, you or your lawyer acting on your behalf may ask the Court for permission to speak at the Hearing. To do so, you or your lawyer must submit a Notice of Intention to Appear. The Notice of Intention to Appear must include copies of any papers, exhibits, or other evidence that you (or your lawyer) plan to present to the Court in connection with the Final Approval Hearing. Your Notice of Intention to Appear must be mailed to Class Counsel and Defendants' Counsel so that it is **post-marked no later than _____,** and it must be **filed** with the Clerk of Court by that same date. See Question 23 for the addresses. You cannot speak at the Hearing if you do not submit an objection and Notice of Intention to Appear, or if you excluded yourself from the Settlement.

IF YOU DO NOTHING

28. What happens if I do nothing at all?

If you do nothing, you will get no money from this Settlement but will remain bound by its terms. **To receive a payment, you must complete and submit a qualifying Settlement Claim Form by _____. See Question 11.**

GETTING MORE INFORMATION

29. How do I get more information about the Settlement?

You may obtain additional information by:

- Calling the Claims Administrator toll-free at 1-___-___-____ to ask questions and receive copies of documents, e-mailing the Claims Administrator at _____.

- Writing to the Claims Administrator at the following address:

  _____
  P.O. Box _____
  _____, __ _____

- Visiting the Settlement website at www._____.com, where you will find answers to common questions about the Settlement plus other information to help you.
- Reviewing legal documents that have been filed with the Clerk of Court in this lawsuit at the Court offices stated in Question 25 above during regular office hours.
- Contacting Class Counsel listed in Question 23 above.

PLEASE DO NOT CALL THE JUDGE OR THE CLERK OF COURT TO ASK QUESTIONS ABOUT THIS LAWSUIT OR NOTICE.

THE COURT WILL NOT RESPOND TO LETTERS OR TELEPHONE CALLS. IF YOU WISH TO ADDRESS THE COURT, YOU MUST FILE AN APPROPRIATE PLEADING OR MOTION WITH THE CLERK OF COURT IN ACCORDANCE WITH THE COURT'S USUAL PROCEDURES.

CHANGE OF ADDRESS FORM

If you are the intended recipient of this Notice, but your address has changed from the address to which it was sent, you should fill out and return this Change of Address Form and mail it to the Claims Administrator so that it is post-marked by _____ and mailed to the following address:

_____
P.O. Box ____
___, ___ _____

Alternatively, you may fill out a Change of Address Form on the Settlement website, www._____.com, by _____.

If you are a Settlement Class Member's Legally Authorized Representative,* please fill out the form below, and also provide your information on the next page.

Last Name of Settlement Class Member: **First Name:** **Middle Initial:**

Current Mailing Address of Settlement Class Member:

City: **State:** **Zip Code:**

Contact Phone Number of Settlement Class Member:

— —

***These terms are further explained in the attached Notice.**

FOR LEGALLY AUTHORIZED REPRESENTATIVES

Fill out this page only if you are filling out the Change of Address Form on behalf of a Settlement Class Member as that Settlement Class Member's Legally Authorized Representative.

(a) Are you the personal representative of a deceased Settlement Class Member? Yes O No O

If so, provide the date of the Settlement Class Member's death: ☐☐ / ☐☐ / ☐☐☐☐

(b) Are you a guardian, conservator, or attorney in fact of an incapacitated Settlement Class Member? Yes O No O

(c) Are you, or are you an agent of a claim filing service, or similar service purporting to act on behalf of an individual Settlement Class Member or group of Settlement Class Members? Yes O No O

Please provide **YOUR** information:

Last Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

First Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Mailing Address ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

City ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

State ☐☐

Zip Code ☐☐☐☐☐

Contact Phone Number: ☐☐☐ – ☐☐☐ – ☐☐☐☐

IMPORTANT: If you are submitting this Change of Address Form on behalf of a Settlement Class Member, please also submit with this Form documents to prove that you are authorized to submit this Form on behalf of that Settlement Class Member (for example, estate documents, powers of attorney, death certificates, etc.).

EXHIBIT B

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

KATE WEISSMAN, Plaintiff, v. UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICE, LLC, AND INTERPUBLIC GROUP OF COMPANIES, INC. CHOICE PLUS PLAN, Defendants.	**CIVIL ACTION NO. 1:19-cv-10580** **Consolidated with 1:19-cv-12224; and** **Consolidated with 1:19-cv-12239** **CLASS ACTION**
RICHARD COLE, Plaintiff, v. UNITED HEALTHCARE INSURANCE COMPANY, Defendants.	CIVIL ACTION NO. 1:19-cv-12224
ZACHARY RIZZUTO, Plaintiff, v. UNITED HEALTHCARE INSURANCE COMPANY, UNITED HEALTHCARE SERVICE, INC., and THE HERTZ CUSTOM BENEFIT PROGRAM, Defendants.	CIVIL ACTION NO. 1:19-cv-12239

PROPOSED ORDER GRANTING PLAINTIFFS' UNOPPOSED MOTION FOR PRELIMINARY APPROVAL OF CLASS ACTION SETTLEMENT AND AGREEMENT

This Action involves claims for alleged violations of the Employee Retirement Income Security Act of 1974, 29 U.S.C. §§ 1132(a)(1(B), (a)(3), and (g) ("ERISA") with respect to coverage of Proton Beam Radiation Therapy ("PBRT") for certain types of cancer under Defendants'[1] health insurance plans.[2] The terms of the Settlement are set out in the Settlement Agreement (filed at ECF No. 114-1), fully executed as of May 9, 2025.

Pursuant to the Plaintiffs'[3] Motion, the Court preliminarily considered the Settlement to determine, among other things, whether the Settlement is sufficient to warrant the issuance of notice to members of the proposed Class. Upon reviewing the Settlement Agreement, the exhibits and attachments thereto, Plaintiffs' Motion, and the declaration of counsel, and the matter having come before the Court, it is hereby **ORDERED, ADJUDGED, AND DECREED** as follows:

1. The Court has jurisdiction over the subject matter of the Action, the Class Representatives, the Settlement Class Members, and Defendants.

2. **Preliminary Certification of the Settlement Class.** In accordance with the Settlement Agreement, and pursuant to Rules 23(a) (b)(1) and (b)(2) of the Federal Rules of Civil Procedure, this Court hereby conditionally certifies for settlement purposes only, the following class (the "Class"):

> Persons who, have not properly excluded themselves per the terms of the Agreement and who:

[1] Defendants United Healthcare Insurance Company, United Healthcare Service, Inc., Interpublic Group of Companies, Inc., Choice Plus Plan, and The Hertz Custom Benefit Program ("Defendants").

[2] All capitalized terms not otherwise defined in this Order shall have the same meaning as ascribed to them in the Settlement Agreement filed at ECF No. 114-1.

[3] The Plaintiffs are Kate Weissman, Richard Cole, and Zachary Rizzuto.

> (1) at the time they were covered by an ERISA-governed plan issued or administered by Defendants; (2) were diagnosed with one of three types of cancer at issue (prostate cancer, primary central nervous system cancer, or cervical/gynecological cancer); (3) either (a) obtained PBRT treatment and submitted a post-service claim for PBRT treatment that was denied between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data) or (b) obtained PBRT treatment after a pre-authorization denial between March 26, 2016 and August 28, 2023 for clinical reasons (identified by specific codes in the data); and (4) the PBRT treatment was not paid for by any other commercial, self-funded, or governmental benefits health payor.

3. Pursuant to the Settlement Agreement, and for settlement purposes only, the Court preliminarily finds that:

(a) as required by Fed. R. Civ. P. 23(a)(1), the Class is ascertainable from records Defendants keep with respect to the Plaintiffs' and the Class Members' claims for coverage of PBRT treatment under their health insurance plans, and the Class is so numerous that joinder of all members is impracticable;

(b) as required by Fed. R. Civ. P. 23(a)(2), there are one or more questions of law and/or fact common to the Class;

(c) as required by Fed. R. Civ. P. 23(a)(3), the claims of the Plaintiffs are typical of the claims of the Class that the Plaintiffs seek to certify;

(d) as required by Fed. R. Civ. P. 23(a)(4), that the Plaintiffs will fairly and adequately protect the interests of the Class in that: (i) the interests of the Plaintiffs and the nature of the alleged claims are consistent with those of the Class Members; and (ii) there appear to be no conflicts between or among the Plaintiffs and the Class Members;

(e) as required by Fed. R. Civ. P. 23(b)(1), the prosecution of separate actions by individual members of the Class would create a risk of: (i) inconsistent or varying adjudications as to individual Class Members that would establish incompatible standards of conduct for the parties opposing the claims asserted in this Action; or (ii) adjudications as to individual Class Members that, as a practical matter, would be dispositive of the interests of the other members not parties to the individual adjudications, or substantially impair or impede the ability of such persons to protect their interests;

(f) as required by Fed. R. Civ. P. 23(b)(2), Defendants have acted or refused to act on grounds that apply generally to the Class, so that final injunctive relief is appropriate respecting the Class as a whole; and

(g) as required by Fed. R. Civ. P. 23(g), Class Counsel are capable of fairly and adequately representing the interests of the Class, and that Class Counsel: (i) have done appropriate work identifying or investigating potential claims in the Action; (ii) are experienced in handling ERISA cases and class actions; and (iii) have committed the necessary resources to represent the Class.

4. For purposes of effectuating the Settlement, the Court preliminarily appoints Plaintiffs Kate Weissman, Richard Cole, and Zachary Rizzuto as Class Representatives for the Class.

5. For purposes of effectuating the Settlement, the Court preliminarily appoints the following counsel as Class Counsel for the Class: (i) Arnall Golden Gregory LLP, (ii) Colson Hicks Eidson, (iii) Kantor & Kantor, and (iv) Kozyak, Tropin & Throckmorton LLP. For the purposes of effectuating the Settlement, Class Counsel are authorized to act on behalf of the Class Representatives,

and all other Settlement Class Members with respect to all acts or consents required by or that may be given pursuant to the Settlement Agreement, including all acts that are reasonably necessary to consummate the Settlement, subject to final approval by the Court of the Settlement.

6. **Preliminary Approval of Proposed Settlement.** The Settlement Agreement is hereby preliminarily approved as fair, reasonable, and adequate. This Court preliminarily finds that:

(a) The Settlement was negotiated vigorously and at arm's length, through four in-person mediation sessions with private mediator Ed Oster at Judicate West, by counsel for Defendants, on the one hand, and the Plaintiffs and Class Counsel on behalf of the Class, on the other hand;

(b) Through nearly six years of litigation, Plaintiffs and Class Counsel had sufficient information to evaluate the settlement value of the Action and have concluded that the Settlement is fair, reasonable, and adequate;

(c) If the Settlement had not been achieved, Plaintiffs and the Class faced the expense, risk, and uncertainty of protracted litigation;

(d) The proposed method for providing monetary relief to Settlement Payment Class Members is fair, reasonable, and adequate, taking into account the costs, risks, and delay of litigation, trial, and appeal. The method of distributing the Settlement Payments is efficient, relying on Defendants' records and requiring the timely submission of only a modest Claim Form and supporting documentation for Settlement Class Members. The Settlement terms related to attorneys' fees do not raise any questions concerning fairness of the Settlement, and there are no agreements, apart

from the Settlement, required to be considered under Fed. R. Civ. P. 23(e)(2)(C)(iv). The Settlement amount is within the range of settlement values obtained in similar cases;

(e) At all times, the Plaintiffs and Class Counsel have acted independently of the Defendants and in the interest of the Class; and

(f) The proposed method of distributing the Settlement Payments is fair, reasonable, and adequate.

7. **Final Approval/Fairness Hearing.** A hearing is scheduled for _____, 2025 at ____ a.m. to make a final determination, concerning among other things:

(a) Any objections from Class Members to the Settlement or any aspects of it;

(b) Whether the Settlement merits final approval as fair, reasonable, and adequate;

(c) Whether the Action should be dismissed with prejudice pursuant to the terms of the Settlement;

(d) Whether Class Counsel adequately represented the Class for purposes of entering into and implementing the Settlement;

(e) Whether the proposed method of distributing the Settlement Payments should be granted final approval;

(f) Whether to approve the payment to the Plaintiffs, as set forth in the Settlement Agreement; and

(g) Whether the Attorneys' Fees and Costs and Plaintiffs' service awards requested in Class Counsel's related application(s) are fair and reasonable and should be approved.

8. **Settlement Notice.** The Court approves the Notice of Proposed Settlement of Class Action and Final Approval Hearing attached to the Settlement Agreement as Exhibit A ("Settlement Notice"). The Court finds that the notice form fairly and adequately: (a) describes the terms and effects of the Settlement Agreement and the Settlement, including any monetary relief to which a Settlement Class Member may be entitled to pursue; (b) gives notice to the Class Members of the time and place of the Fairness Hearing; and (c) describes how the recipients of the Settlement Notice may object to any of the relief requested; and (d) describes how the recipients of the Settlement Notice may request to be excluded from the Settlement. Costs associated with the Settlement Administrator will be paid separately from the benefit to the Class.

9. **Settlement Administrator.** The Court hereby approves the appointment of Rust Consulting, Inc. as the Settlement Administrator for the Settlement. The Court directs that the Settlement Administrator shall:

(a) Within 15 days after entry of the Preliminary Approval Order, United Healthcare shall, for purposes of facilitating the distribution of the Summary Settlement Notice, provide the Settlement Administrator with the last known telephone numbers and physical addresses, for all persons that United Healthcare's records reasonably indicate are likely to the Settlement Class Members.

(b) No more than 30 days after the entry of the Preliminary Approval Order, cause the Settlement Notice and Claim Form (Exhibit E to the parties' Settlement Agreement), with such non-substantive modifications thereto as may be agreed upon by the Parties, to be sent via U.S. mail to Settlement Class Members on the Class List. Prior to mailing the Settlement Notice,

the Settlement Administrator shall update the last known addresses reflected in the Defendants' records for the Class List by comparing them to the National Change of Address system to ensure individual notice is provided to all reasonably identifiable Settlement Class Members. If any Settlement Notices are returned as undeliverable with forwarding addresses provided, the Settlement Administrator shall re-send Settlement Notices and Claim Forms to the forwarding addresses. For any Settlement Notices returned undeliverable without forwarding addresses provided, the Settlement Administrator shall run an address search (skiptrace) against a comparable address database, and re-send Settlement Notices and Claim Forms to any updated addresses obtained.

(c) The Court finds that the contents of the Settlement Notice and the process described herein and in the Settlement are appropriate and the best notice practicable under the circumstances, and satisfy the requirements of Rule 23(c) and Due Process.

10. Petition for Attorneys' Fees, Litigation Costs and Plaintiffs' Awards. Any petition by Class Counsel for attorneys' fees, litigation costs and awards to the Named Plaintiffs, and all briefs in support thereof, shall be filed within 35 days of the entry of this Preliminary Approval Order.

11. Briefs in Support of Final Approval of the Settlement. Briefs and other documents in support of final approval of the Settlement shall be filed at least 21 days prior to the Final Approval Hearing. Any reply briefs in support of final approval of the Settlement shall be filed no later than 7 days prior to the Final Approval Hearing.

12. Objections to Settlement — Any Class Member who wishes to object to the Settlement may submit a written notice of objection to be considered by the Court in advance of the Fairness Hearing. If a Class Member wishes to submit a written objection to the Settlement, the written objection must be postmarked no later than forty-five (45) calendar days from the date the Settlement Notice was sent to the Class Members. To submit a written objection, a Class Member must deliver a notice of objection to Class Counsel and Defendants' Counsel at the addresses identified in the Settlement Notice (¶ 23). The notice of objection must: (i) identify the case name and number; (ii) identify the person submitting the objection as a Class Member; (iii) attach copies of materials the Class Member will submit to the Court or present at the Fairness Hearing (if any); (iv) be signed by the Class Member; and (v) clearly state in detail: (1) the legal and factual ground(s) for the objection; (2) the Class Member's name, address, and, if available, telephone number; and (3) if represented by counsel, such counsel's name, address, and telephone number. If a Class Member submits a written objection to the Settlement before the Court-approved deadline, they may also attend the Fairness Hearing to present their objections to the Court. They may attend the Fairness Hearing even if they do not file a written objection, but they will only be allowed to speak at the Fairness Hearing if they file a written objection in advance of the hearing, subject to the discretion of the Court.

13. **Opting Out.** Any Settlement Payment Class Member who does not wish to participate in the Settlement Payment Class (i.e., "opt out") must do so in writing, which shall be mailed to the Settlement Administrator. Such opt out requests must be postmarked no later than forty-five (45) days from the date the Settlement Notice was sent to the Class. The request must (1) identify the case name and number; (2) be signed by the person seeking to be excluded from the Settlement Payment Class; (3) clearly express the person's desire to be excluded from the Settlement Payment Class; and

(4) include the person's name, address, and, if available, telephone number, and, if represented by counsel, counsel's name, address, and telephone number. Any Settlement Class Member who wishes to be excluded from the Settlement Payment Class can only opt out for himself or herself and cannot opt out for any other person or any group of persons (with the exception of a person acting on behalf of Settlement Class Members), nor can any person within the Settlement Class authorize any other person to opt out on his or her behalf (with the exception of a caregiver or conservator acting on behalf of a Settlement Class Member who requires such assistance, who must provide evidence of their authority to act on behalf of the Settlement Class Member). Any request for exclusion that fails to satisfy these requirements, or that has not been timely postmarked shall be deemed ineffective, and any person included within the Settlement Class who does not properly and timely submit a request for exclusion shall be deemed to have waived all rights to opt out and shall be deemed a Settlement Class Member for all purposes under the Agreement. Any additional briefs the Parties may wish to file in support of the Settlement shall be filed at least 7 days prior to the Fairness Hearing.

14. Parallel Proceedings — Pending final determination of whether the Settlement Agreement should be approved, the Plaintiffs and the Class Members are prohibited and enjoined from directly, through representatives, or in any other capacity, commencing any action or proceeding in any court or tribunal asserting any of the Released Claims against the Released Parties, including Defendants. This provision does not apply to any actions a Class Member may have brought against Defendants prior to the date of this Order.

15. Class Action Fairness Act Notice. The form of notice under the Class Action Fairness Act of 2005 ("CAFA") submitted along with the request for preliminary approval of the Settlement Agreement complies with the requirements of CAFA.

16. Continuance of Final Approval/ Fairness Hearing. The Court reserves the right to continue the Fairness Hearing without further written notice to the Class Members and also may schedule the hearing to be conducted by telephone or video conference.

SO ORDERED this ___ day of May 2025.

Dated: May_____, 2025

/s/_____
ALLISON D. BURROUGHS
U.S. DISTRICT JUDGE

EXHIBIT C

THE PARTIES WILL SEPARATELY FILE THE PROPOSED FINAL APPROVAL ORDER AND JUDGMENT.

EXHIBIT D

Proton Beam Radiation Therapy

Policy Number: 2023T0132FF
Effective Date: October 1, 2023

Instructions for Use

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Related Commercial/Individual Exchange Policies

- Intensity-Modulated Radiation Therapy
- Radiation Therapy: Fractionation, Image-Guidance, and Special Services
- Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery

Community Plan Policy

- Proton Beam Radiation Therapy

Medicare Advantage Coverage Summary

- Radiation and Oncologic Procedures

Application

UnitedHealthcare Commercial

This Medical Policy applies to all UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans in all states except for Colorado.

Coverage Rationale

Note: This policy applies to persons 19 years of age and older. Proton beam radiation therapy (PBRT, PBT) is covered without further review for persons younger than 19 years of age.

The following are proven and medically necessary:

- PBT for Definitive Therapy of the following indications:
  - Hepatocellular carcinoma (HCC) (localized, unresectable) in the curative setting when documentation is provided that sparing of the surrounding normal tissue cannot be achieved with standard radiation therapy techniques, including intensity-modulated radiation therapy (IMRT), and stereotactic body radiation therapy (SBRT), and selective internal radiation spheres, and transarterial therapy (for example, chemoembolization) is contraindicated or not technically feasible
  - Intracranial arteriovenous malformations (AVMs)
  - Ocular tumors, including intraocular/uveal melanoma (includes the iris, ciliary body and choroid)
  - Skull-based tumors (e.g., chordomas, chondrosarcomas, paranasal sinus or nasopharyngeal tumors)

- ~~PBT may be covered for a diagnosis that is not listed above as proven, including recurrences or metastases in selected cases. Requests for exceptions will be evaluated on a case-by-case basis when both of the following criteria are met:~~
  - ~~Documentation is provided that sparing of the surrounding normal tissue cannot be achieved with standard radiation therapy techniques; and~~
  - ~~Evaluation includes a comparison of treatment plans for PBT, IMRT and SBRT~~

PBT and IMRT are proven and considered clinically equivalent for treating prostate cancer. Medical necessity will be determined based on the terms of the member's benefit plan.

PBT is unproven and not medically necessary due to insufficient evidence of efficacy for treating all other indications; however, PBT may be covered for a diagnosis that is not listed above as proven, including recurrences or metastases in selected cases. Requests for exceptions will be evaluated on a case-by-case basis when both of the following criteria are met:

- Documentation is provided that sparing of the surrounding normal tissue cannot be achieved with standard radiation therapy techniques; and
- Evaluation includes a comparison of treatment plans for PBT, IMRT and SBRT for the specific member

~~**not listed above as proven, including but not limited to:**~~

- ~~Age related macular degeneration (AMD)~~
- ~~Bladder cancer~~
- ~~Brain and spinal cord tumors~~
- ~~Breast cancer~~
- ~~Choroidal hemangioma~~
- ~~Esophageal cancer~~
- ~~Gynecologic cancers~~
- ~~Head and neck tumors not noted above as proven~~
- ~~Lung cancer~~
- ~~Lymphomas~~
- ~~Pancreatic cancer~~
- ~~Vestibular tumors (e.g., acoustic neuroma or vestibular schwannoma)~~
- ~~PBT used in conjunction with IMRT~~

Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

CPT/HCPCS Codes*	Required Clinical Information
Proton Beam Radiation Therapy (PBT)	
77385, 77386, 77387, 77520, 77522, 77523, 77525, G6015, G6016	Medical notes documenting the following, when applicable: History of medical condition requiring treatment • Documentation that sparing of the surrounding normal tissue cannot be achieved with standard • radiation therapy techniques Evaluation includes a comparison of treatment plans for PBT, IMRT, and stereotactic body radiation • therapy (SBRT) for the specific member • For hypofractionated radiation, provide the prescribed total dose and dose per fraction • For delivery of radiation therapy course with standard fractionation, provide the dose prescription along with documentation in the form of a clearly labeled, color comparative proton, and IMRT dose volume histogram and dose table, in absolute doses noting that sparing of the surrounding normal tissue cannot be achieved with IMRT techniques **Note**: If citing an RTOG dose constraint, provide the RTOG protocol number • Physician's treatment plan **Note**: The color comparative proton and IMRT dose volume histogram and dose table images can be submitted via the external portal at http://www.uhcprovider.com/paan; faxes of images will not be accepted.

*For code descriptions, refer to the Applicable Codes section.

Definitions

Definitive Therapy: Definitive Therapy is treatment with curative intent. Treatment of a local recurrence of the primary tumor may be considered "Definitive" if there has been a long disease-free interval (generally ≥ 2 years) and treatment is with curative intent.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
77385	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
77386	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex
77387	Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
77520	Proton treatment delivery; simple, without compensation
77522	Proton treatment delivery; simple, with compensation
77523	Proton treatment delivery; intermediate
77525	Proton treatment delivery; complex

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HCPCS Code	Description
G6015	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session
G6017	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

Diagnosis Code	Description
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C22.0	Liver cell carcinoma
C30.0	Malignant neoplasm of nasal cavity

Diagnosis Code	Description
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C31.2	Malignant neoplasm of frontal sinus
C31.3	Malignant neoplasm of sphenoid sinus
C31.8	Malignant neoplasm of overlapping sites of accessory sinuses
C31.9	Malignant neoplasm of accessory sinus, unspecified
C41.0	Malignant neoplasm of bones of skull and face
C61	Malignant neoplasm of prostate
C69.0	Malignant neoplasm of conjunctiva
C69.00	Malignant neoplasm of unspecified conjunctiva
C69.01	Malignant neoplasm of right conjunctiva
C69.02	Malignant neoplasm of left conjunctiva
C69.1	Malignant neoplasm of cornea
C69.10	Malignant neoplasm of unspecified cornea
C69.11	Malignant neoplasm of right cornea
C69.12	Malignant neoplasm of left cornea
C69.20	Malignant neoplasm of unspecified retina
C69.21	Malignant neoplasm of right retina
C69.22	Malignant neoplasm of left retina
C69.30	Malignant neoplasm of unspecified choroid
C69.31	Malignant neoplasm of right choroid
C69.32	Malignant neoplasm of left choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.41	Malignant neoplasm of right ciliary body
C69.42	Malignant neoplasm of left ciliary body
C69.50	Malignant neoplasm of unspecified lacrimal gland and duct
C69.51	Malignant neoplasm of right lacrimal gland and duct
C69.52	Malignant neoplasm of left lacrimal gland and duct
C69.6	Malignant neoplasm of orbit
C69.60	Malignant neoplasm of unspecified orbit
C69.61	Malignant neoplasm of right orbit
C69.62	Malignant neoplasm of left orbit
C69.8	Malignant neoplasm of overlapping sites of eye and adnexa
C69.80	Malignant neoplasm of overlapping sites of unspecified eye and adnexa
C69.81	Malignant neoplasm of overlapping sites of right eye and adnexa
C69.82	Malignant neoplasm of overlapping sites of left eye and adnexa
C69.9	Malignant neoplasm of unspecified site of eye
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
D09.20	Carcinoma in situ of unspecified eye
D09.21	Carcinoma in situ of right eye

Diagnosis Code	Description
D09.22	Carcinoma in situ of left eye
D14.0	Benign neoplasm of middle ear, nasal cavity and accessory sinuses
D16.4	Benign neoplasm of bones of skull and face
D31.30	Benign neoplasm of unspecified choroid
D31.31	Benign neoplasm of right choroid
D31.32	Benign neoplasm of left choroid
D31.40	Benign neoplasm of unspecified ciliary body
D31.41	Benign neoplasm of right ciliary body
D31.42	Benign neoplasm of left ciliary body
Q28.2	Arteriovenous malformation of cerebral vessels
Q28.3	Other malformations of cerebral vessels

Description of Services

Unlike other types of radiation therapy (RT) that use x-rays or photons to destroy cancer cells, proton beam therapy (PBT) uses a beam of special particles (protons) that carry a positive charge. There is no significant difference in the biological effects of protons versus photons; however, protons can deliver a dose of radiation in a more confined way to the tumor tissue than photons. After they enter the body, protons release most of their energy within the tumor region and, unlike photons, deliver only a minimal dose beyond the tumor boundaries (American College of Radiology (ACR) website, updated 2021).

Proton beam radiation therapy (PBRT) is intended to deliver higher, more targeted radiation with less damage to collateral healthy tissue than external beam radiation therapy (EBRT) using photons (x-rays) when used to treat solid tumors. While PBRT has been used for several solid cancer tumor types (e.g., breast, lung, prostate, head and neck, central nervous system (CNS)) in adults and in certain pediatric cancers, evidence is lacking regarding clear benefits over EBRT (ECRI, 2017).

Clinical Evidence

Proven Indications

Hepatocellular Carcinoma (HCC)

In a randomized phase III trial (NCT01963429), Kim et al. (2021) compared the outcomes of PBT and radiofrequency ablation (RFA) in patients with recurrent/residual HCC (size < 3 cm, number ≤ 2). The primary endpoint was 2-year local progression-free survival (LPFS), with a non-inferiority margin of 15% in the per-protocol (PP) population. Complementary analysis was performed in the intention-to-treat (ITT) population. Patients were randomly assigned to receive PBT or RFA according to tumor stage and Child-Pugh score. Crossover was permitted after randomization if the assigned treatment was technically possible. The ITT population included 144 patients, PBT (n = 72) or RFA (n = 72). Nineteen patients switched from the RFA arm to the PBT arm, and six patients switched from the PBT arm to RFA. In the PP population, the 2-year LPFS rate with PBT (n = 80) vs. RFA (n = 56) was 94.8% vs. 83.9%, a difference of 10.9 percentage points ($p < 0.001$); in the ITT population, the 2-year LPFS rate with PBT vs. RFA was 92.8% vs. 83.2%, a difference of 9.6 percentage points ($p < 0.001$), meeting the criteria for non-inferiority. The 3- and 4-year LPFS rates for PBT were also non-inferior to those for RFA. The most common adverse events were radiation pneumonitis (32.5%) and decreased leukocyte counts (23.8%) for PBT and increased alanine aminotransferase levels (96.4%) and abdominal pain (30.4%) for RFA. No Grade 4 adverse events or mortality were noted. The authors concluded PBT is associated with LPFS rates that are comparable to those observed for RFA in patients with recurrent/residual HCC. PBT was also tolerable and safe. Limitations noted by the authors include the primary outcome measure of 2-year LPFS, rather than progression-free survival (PFS) or overall survival (OS), single-center design, and most patients had chronic hepatitis B. The authors recommend further studies across other institutions including patients with various etiologies.

Parzen et al. (2021) conducted a nine-institution multicenter study to evaluate the safety and efficacy of hypofractionated PBT for HCC and intrahepatic cholangiocarcinoma (ICC). The study evaluated the prospective registry of the Proton Collaborative Group for patients undergoing definitive PBT for liver tumors. Information compiled included demographic, clinicopathic,

toxicity and dosimetry data. Between 2013 and 2019, 63 patients were treated, 30 patients had HCC and 25 had ICC. The median dose and biological equivalent dose (BED) delivered was 58.05 GyE and 80.5 GyE, respectively. The median mean liver BED was 13.9 GyE. At least one grade ≥ 3 toxicity was experienced by three patients. With median follow-up of 5.1 months the local control (LC) rate at 1 year was 91.2% for HCC and 90.9% for ICC. The 1-year LC was significantly higher (95.7%) for patients receiving BED greater than 75.2 GyE than for patients receiving BED of 75.2 GyE or lower (84.6%, p = 0.029). The OS rate at 1 year was 65.6% for HCC and 81.8% for ICC. The authors concluded hypofractionated PBT resulted in low toxicity, sparing of the uninvolved liver, and excellent LC, even in the setting of dose-escalation. The study found higher dose correlated with improved LC. Limitations include lack of comparison group and limited follow-up time.

Fukuda et al. (2017) performed an observational study to assess the long-term efficacy of PBT in patients with previously untreated HCC. Between January 2002 and December 2009, 129 patients at a single institution received PBT via one of three protocols based on tumor location with dose volumes of 77.0 GyE in 35 fractions, 72.6 GyE in 22 fractions and 66.0 GyE in 10 fractions for the gastrointestinal (GI), hilar and standard protocols, respectively. Primary outcome measures were local tumor control (LTC), OS, and PFS. All 129 patients completed PBT without experiencing severe complications, and no treatment-related deaths were observed. The median patient observation period was 55 months. The 5-year LTC, PFS, and OS rates were 94%, 28%, and 69% for patients with 0/A stage disease (n = 9/21), 87%, 23%, and 66% for patients with B stage disease (n = 34), and 75%, 9%, and 25% for patients with C stage disease (n = 65), respectively. The 5-year LTC and OS rates of fifteen patients with tumor thrombi in major vessels were 90% and 34%, respectively. The major study limitation cited was the heterogeneous patient population, with most subjects selecting receiving PBT because they refused surgery or conventional interventional RT. The authors concluded that PBT achieved long term tumor control with less toxicity and is a viable treatment option for localized HCC. The authors are now planning a multicenter controlled study comparing PBT and hepatectomy.

Bush et al. (2016) conducted a single-center, prospective random controlled trial (RCT), comparing outcomes of 69 patients with newly diagnosed HCC who received either trans arterial chemoembolization (TACE) or PBT as definitive or bridge therapy while awaiting transplantation. Thirty-three subjects were randomized to PBT, and 36 subjects were randomized to TACE, Patients randomized to TACE received at least one TACE with additional TACE for persistent disease. The PBT group had proton therapy delivered to all areas of gross disease to a total dose of 70.2 Gy in 15 daily fractions over three weeks. The median follow-up for all subjects was 28 months. The primary endpoint was PFS, with secondary endpoints including OS, local disease control, transplant outcomes, and toxicity including days of hospitalization after treatment. The 2-year OS for the entire group was 59%, with no significant difference between treatment assignments. Regarding local control and PFS between treatment groups, there was a trend toward improved 2-year LTC (88% vs 45%, p = .06) and PFS (48% vs 31%, p = .06) favoring the PBT group. For the entire group of study subjects, 22 went on to have liver transplantation. The 2-year OS after transplantation was 82% for the entire group, with no difference seen between proton and TACE groups. The authors concluded that this study indicates similar OS rates for PBT and TACE. While there is a trend toward improved local tumor control and PFS favoring proton therapy, it is too early to determine whether this trend will be maintained.

Hong et al. (2016) conducted a single-arm, phase II, multi-institutional study to evaluate the safety and efficacy of high-dose, hypofractionated PBT for HCC and ICC. Eighty-three participants ≥ 18 years with unresectable or locally recurrent HCC or ICC were included. With 42 HCC patients (95.5%) and 36 ICC patients (92.3%) having completed their prescribed dose, the median dose delivered was 58.0 GyE (in 15 fractions; range, 15.1 to 67.5 GyE). Of the 83 patients, 71 (85.5%) experienced at least one radiation-related toxicity event while in the study, most commonly fatigue (54/83, 65.1%), rash (51/83, 61.4%), nausea (25/83, 30.1%), or anorexia (21/83, 25.3%). Median follow-up among the 50 survivors was 19.5 months (range, 0.6 to 55.9 months). For patients with HCC, the 1-year and 2-year PFS rates were 56.1% and 39.9%, respectively. The 1- and 2-year OS was 76.5% and 63.2%, respectively. Three patients with HCC underwent successful liver transplantation, two of whom remain alive. For patients with ICC, 1-year and 2-year PFS rates were 41.4% and 25.7%, respectively; with 1-year and 2-year OS rates of 69.7% and 46.5%, respectively. The authors concluded that high-dose, hypofractionated PBT is safe and associated with high rates of LC and OS for both HCC and ICC. These data provide the strong rationale for RCTs of proton versus photon RT for HCC, and for chemotherapy with or without RT for ICC.

A phase III randomized trial comparing PBT to radiofrequency ablation (NCT02640924) was in progress, but the study has passed its completion date and status has not been verified in more than two years. Another clinical trial that compares protons to photons (NCT03186898) is in the recruiting stage. For more information on this and other clinical trials studying PBT and HCC, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

An ASTRO clinical practice guideline states that for patients with HCC receiving dose-escalated ultra- or moderately hypofractionated EBRT, IMRT or proton therapy is strongly recommended, with choice of regimen based on tumor location, underlying liver function, and available technology. For patients with unresectable intrahepatic cholangiocarcinoma (IHC) receiving dose-escalated ultra- or moderately hypofractionated EBRT, IMRT or proton therapy is conditionally recommended with choice of regimen based on tumor location, underlying liver function, and available technology (Apisarnthanarax et al., 2022).

National Comprehensive Cancer Network (NCCN)

NCCN guidelines state that hypofractionation with photons or protons at an experienced center is an acceptable option for unresectable intrahepatic tumors (NCCN, 2022).

Intracranial Arteriovenous Malformations (AVM)

Zuurbier et al. (2019) updated a previously conducted systematic review (Ross, 2010) that aimed to determine the effectiveness and safety of the different interventions, alone or in combination, for treating brain AVMs in adults compared against either each other, or conservative management, in RCTs. A search was conducted using the Cochrane Stroke Group Trials Register, the Cochrane Central Register of Controlled Trials, the Cochrane Library, MEDLINE, OVID and Embase OVID. The search identified fourteen eligible RCTs and of those, thirteen were excluded (ten did not meet the inclusion criteria and three were still ongoing), and one RCT with 226 participants was included (Mohr, 2013). The study titled, A Randomized trial of Unruptured Brain Arteriovenous malformations (ARUBA) was an international, multi-center, randomized, controlled, open, prospective clinical trial comparing interventional treatment (endovascular, surgical, and/or radiation therapy) to conservative management for unruptured brain AVMs in adults. The primary outcome was death or dependence from any cause (modified Rankin Scale score ≥ 2), and secondary outcomes included symptomatic intracranial hemorrhage, epileptic seizure, symptomatic radiation necrosis detected by MRI, and quality of life (QOL). Data on functional outcome and death at twelve months of follow-up were provided for 218 (96%) of the participants. Intervention compared to conservative management increased death or dependency with a risk ratio (RR) of 2.53, 95% CI 1.28 to 4.98, and higher proportion of participants with symptomatic intracranial hemorrhage (RR 6.75, 95% CI 2.07 to 21.96). There was no difference in the frequency of epileptic seizures (RR 1.14, 95% CI 0.63 to 2.06). The authors reported that moderate-quality evidence from one RCT (of adults with unruptured brain AVMs) showed that conservative management was superior to intervention with respect to functional outcome and symptomatic intracranial hemorrhage during the 1-year period after randomization however, more RCTs are needed to confirm or refute these findings.

Blomquist et al. (2016) performed a retrospective review of 65 patients with AVMs treated with PBT. Information collected from patient medical records, treatment protocols and radiological results included gender, age, presenting symptoms, clinical course, and AVM nidus size and rate of occlusion. Outcome parameters were the occlusion of the AVM, clinical outcome and side effects. The overall rate of occlusion was 68%. For target volume 0-2 cm^3 it was 77%, for 3-10 cm^3 80%, for 11-15 cm^3 50% and for 16-51 cm^3 20%. Those with total regress of the AVM had significantly smaller target volumes ($p < 0.009$) higher fraction dose ($p < 0.001$) as well as total dose ($p < 0.004$) compared to the rest. The target volume was an independent predictor of total occlusion ($p = 0.03$). There was no difference between those with and without total occlusion regarding mean age, gender distribution or symptoms at diagnosis. Mild radiation-induced brain edema developed in 41 patients and was more common in those that had total occlusion of the AVM. Brain hemorrhage after treatment was experienced by two patients. Two thirds of those presenting with seizures reported an improved seizure situation after treatment. The authors concluded that PBT is a treatment alternative for brain AVMs due to the high occlusion rate even in large AVMs. Limitations include the retrospective study design, lack of comparative group and small study size.

Hattangadi-Gluth et al. (2014) evaluated the obliteration rate and potential AEs of single-fraction proton beam stereotactic radiosurgery (PSRS) in patients with cerebral AVMs. From 1991 to 2010, 248 consecutive patients with 254 cerebral AVMs received single-fraction PSRS at a single institution. The median AVM nidus volume was 3.5 cc, 23% of AVMs were in critical/deep locations (basal ganglia, thalamus or brainstem) and the most common dose was fifteen Gy. At a median follow-up time of 35 months, 64.6% of AVMs were obliterated. The median time to total obliteration was 31 months, and the 5- and 10-year cumulative incidence of total obliteration was 70% and 91%, respectively. On univariable analysis, smaller target volume, smaller treatment volume, higher prescription dose and higher maximum dose were associated with total obliteration.

Deep/critical location was also associated with decreased likelihood of obliteration. On multivariable analysis, critical location and smaller target volume remained associated with total obliteration. Post-treatment hemorrhage occurred in thirteen cases (5-year cumulative incidence of 7%), all among patients with less than total obliteration. Three of these events were fatal. The most common complication was seizure. The authors reported that this is the largest modern series of PSRS for cerebral AVMs and concluded that PSRS can achieve a high obliteration rate with minimal morbidity. Post-treatment hemorrhage remains a potentially fatal risk among patients who have not yet responded to treatment.

Hattangadi et al. (2012) evaluated 59 patients with high-risk cerebral AVMs, based on brain location or large size, who underwent planned two-fraction PSRS. Median nidus volume was 23 cc. Seventy percent of cases had nidus volume ≥ 14 cc, and 34% were in critical locations (brainstem, basal ganglia). Many patients had prior surgery or embolization (40%) or prior PSRS (12%). The most common dose was sixteen Gy in 2 fractions. At a median follow-up of 56.1 months, nine patients (15%) had total and twenty patients (34%) had partial obliteration. Patients with total obliteration received higher total dose than those with partial or no obliteration. Median time to total obliteration was 62 months, and 5-year actuarial rate of partial or total obliteration was 33%. Five-year actuarial rate of hemorrhage was 22% and 14% (n = 8) suffered fatal hemorrhage. Lesions with higher AVM scores were more likely to hemorrhage and less responsive to radiation. The most common complication was headache. One patient developed a generalized seizure disorder, and two had mild neurologic deficits. The authors concluded that high-risk AVMs can be safely treated with 2-fraction PSRS, although total obliteration rate is low, and patients remain at risk for future hemorrhage. Future studies should include higher doses or a multistage PSRS approach for lesions more resistant to obliteration with radiation.

Ocular Tumors

Hartsell et al. (2016) conducted a case series study to determine feasibility of treating patients with ocular melanoma using volumetric imaging and planning for PBT. Twenty-six patients met eligibility criteria, and all were able to complete and tolerate treatment. Visual outcomes were assessed on routine ophthalmologic follow-up over a median time frame of 31 months. Four patients had poor vision in the treated eye prior to PBT; three of those four patients had serous retinal detachment prior to treatment. None of those patients had significant improvement in visual acuity after treatment. Of the remaining 22 patients, nine had visual acuity equal to pre-treatment acuity at the most recent follow-up visit, four had stable vision with a loss of two to five lines on the Snellen chart, and eight patients had lost more than five lines of visual acuity. The visual acuity status for one patient was unknown prior to his death from metastatic melanoma. The treatment was well tolerated by patients with minimal acute toxicity. Relatively low mean doses to the anterior structures (ciliary body and lens) were maintained, even in patients with large tumors. The authors concluded that while they continue evaluating outcomes of these patients in a prospective manner, this treatment technique appears to be feasible with excellent early outcomes.

Verma and Mehta (2016c) conducted systematic review to identify studies on PBT and uveal melanoma. The search was conducted using PubMed, EMBASE, abstracts from meetings of the American Societies for Radiation Oncology and Clinical Oncology, and the Particle Therapy Co-Operative Group. Articles included addressed clinical outcomes of proton radiotherapy for ocular melanoma with the following headings: proton, proton radiation therapy, proton beam therapy, ocular melanoma, uveal melanoma, choroidal melanoma, eye melanoma, and were published from 2000 to 2015. Articles excluded were those without specific assessments on clinically relevant outcomes of proton radiotherapy for previously untreated melanoma of the eye, letters to the editor, direct commentary to other articles, and small reports (< 25 patients). A total of fourteen original investigations from 10 institutions were analyzed. Results revealed that the majority of tumors were choroidal and medium to large-sized, and received 50–70 Gy equivalent doses however, more recent data reported use of lower doses. The five-year local control rates exceeded 90% and remained high at fifteen years. The 5-year OS rates ranged from 70–85%, and 5-year metastasis-free survival and disease-specific survival rates ranged from 75-90%, with more recent series reporting higher values. With the removal of smaller studies, 5-year enucleation rates were consistently between seven and ten percent. Many patients (60–70%) showed a post-PBT visual acuity decrease but still retained purposeful vision (> 20/200). Complication rates were variable but showed improvements compared with historical plaque brachytherapy data. The authors concluded that PBT has shown excellent oncological and ophthalmological outcomes, and these have been sustained in the long-term.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's model policy states PBT is considered reasonable in instances where sparing the surrounding tissue cannot be adequately achieved with photon-based radiotherapy and is of added clinical benefit to the patient. Disease sites that frequently

support the use of PBT include treatment of ocular tumors, including intraocular melanomas (2017). (Accessed September 13, 2022).

National Comprehensive Cancer Network (NCCN)

In the NCCN guidelines on uveal melanoma, particle beam therapy is noted as a common form of definitive RT for the primary tumor. It is considered appropriate as an upfront therapy after initial diagnosis, after margin-positive enucleation, or for intraocular or orbital recurrence. It should be performed by an experienced multidisciplinary team including an ophthalmic oncologist, radiation oncologist, and particle beam physicist (NCCN, 2022).

Prostate Cancer

An ECRI Clinical Evidence Assessment for PBT and localized prostate cancer concluded PBT is relatively safe for treatment of prostate cancer; however, it is unclear whether PBT is more effective than photon EBRT or brachytherapy, or has fewer adverse effects or complications (2022).

Vapiwala et al. (2021) conducted a multi-institutional analysis that compared late toxicity profiles of patients with early-stage prostate cancer treated with moderately hypofractionated PBT and IMRT. The study included patients (n = 1850) with low- or intermediate-risk biopsy-proven prostate adenocarcinoma treated from 1998 to 2018. The patients were treated with moderately hypofractionated radiation, defined as 250 to 300 cGy per daily fraction given for four to six weeks, and stratified by use of IMRT or PBT. Late genitourinary (GU) and gastrointestinal (GI) toxicity were the primary outcomes. Adjusted toxicity rates were calculated using inverse probability of treatment weighting, accounting for race, National Comprehensive Cancer Network risk group, age, pretreatment International Prostate Symptom Score (GU only), and anticoagulant use (GI only). Of the 1850 patients included, 1282 had IMRT and 568 had PBT. The majority of patients experienced no late GU or GI toxicity, with late grade 3 + GU toxicity of 2.0% versus 3.9% and late grade 2 + GI toxicity of 14.6% versus 4.7% for the PBT and IMRT cohorts, respectively. Only anticoagulant use was significantly predictive of GI toxicity and no factors were significantly predictive of GU toxicity. The authors concluded that treatment with moderately hypofractionated IMRT and PBT resulted in low rates of toxicity in patients with early-stage prostate cancer. No difference was seen in late GI and GU toxicity between the modalities during long-term follow-up and both treatments were well tolerated and safe.

A Hayes report assessed 20 studies, including four RCTs, two prospective cohort studies, two retrospective registry analysis studies, and twelve retrospective comparative or case-matched cohort studies that evaluated the efficacy and safety of PBT in patients with localized or locally advanced prostate cancer. The report concludes that the best available studies of PBT for localized prostate cancer have consistently found that most or nearly all patients remain free from cancer progression for five years or longer after treatment. These results are promising but none of the reviewed studies assessed the efficacy of PBT as the sole or primary therapy for prostate cancer relative to the efficacy of other common methods of RT. Ten of the reviewed studies found that the safety of PBT as sole or primary therapy was usually similar to the safety of other common RT; however, these studies are of low quality since they were retrospective. Moreover, these ten studies do not provide sufficient evidence of comparative safety since they were divided between evaluations of PBT relative to brachytherapy, conformal X-ray therapy, and IMRT. The other available studies do not provide clear evidence concerning the relative safety and efficacy of PBT for prostate cancer since these other studies evaluated it as an adjunct to X-ray therapy or did not compare it with another common RT. Additional well-designed studies are needed to establish the clinical role of PBT relative to other widely used therapies for localized prostate cancer (2020, Updated 2022).

Santos et al. (2019) compared acute and late GU and GI toxicity outcomes in patients with prostate cancer who received treatment with postprostatectomy IMRT versus PBT. Patients with prostate cancer who received adjuvant or salvage IMRT or PBT (70.2 gray with an endorectal balloon) after prostatectomy from 2009 through 2017 were reviewed. A case-matched cohort analysis was performed using nearest-neighbor 3-to-1 matching by age, and GU/GI disorder history. The Kaplan-Meier method was used to assess toxicity-free survival (TFS). Seventy matched pairs were generated from the 307 men identified (IMRT, n = 237, PBT, n = 70). The median follow-up was 48.6 and 46.1 months for the IMRT and PBT groups, respectively. While PBT was superior at reducing low-range (volumes receiving 10% to 40% of the dose, respectively) bladder and rectal doses (all $p \leq .01$), treatment modality was not associated with differences in clinician-reported acute or late GU/GI toxicities (all $p \geq .05$). Five-year grade ≥ 2 GU and grade ≥1 GI TFS was 61.1% and 73.7% for IMRT, respectively, and 70.7% and 75.3% for PBT, respectively; and 5-year grade ≥ 3 GU and GI TFS was > 95% for both groups (all $p \geq .05$). The authors concluded that postprostatectomy PBT minimized low-range bladder and rectal dose relative to IMRT; however, treatment modality was not associated with clinician-reported GU/GI toxicities. The authors recommended future prospective studies and on-going follow-up to determine

whether dosimetric differences between IMRT and PBT lead to clinically meaningful differences in long-term outcomes. Limitations include lack of randomization and retrospective study design.

Several single-institution studies report favorable clinical outcomes of PBT in prostate cancer. Henderson et al. (2017) reported 5-year outcomes of a prospective trial of image-guided accelerated hypofractionated proton therapy (AHPT) for prostate cancer from a single institution. Late radiation AEs/toxicities and freedom from biochemical and/or clinical progression (FFBP) were the outcome measurements for the 215 participants categorized as low and intermediate risk. Median follow-up was 5.2 years, with FFBP rates overall noted at 95.9%. For the subsets of low and intermediate risk, FFBP was 98.3% and 92.7%, respectively. Actuarial 5-year rates of significant ($\geq$ grade 3) late radiation-related GI AEs/toxicities were 0.5%, and 1.7% for GU AEs.

Bryant et al. (2016) performed a single-center study on 1,327 men with localized prostate cancer who received image guided PBT between 2006-2010. The 5-year FFBP rates were 99% for low-risk, 94% for intermediate-risk, and 76% for high-risk patients. The authors concluded that PBT provided excellent control of disease with low rates of GU/GI toxicity. Large prospective comparative studies with longer follow-up times are necessary for a true comparison between PBT and other types of RT.

In a case-matched analysis, Fang et al. (2015) assessed prospectively collected toxicity data on patients with localized prostate cancer who received treatment with IMRT and PBT techniques and similar dose-fractionation schedules. A total of 394 patients were treated with either PBT (n = 181) or IMRT (n = 213). Patients were case-matched on risk group, age and prior GI and GU disorders, resulting in 94 matched pairs. The risks of acute and late GI/GU toxicities did not differ significantly after adjustment for confounders and predictive factors.

Mendenhall et al. (2014) reported 5-year clinical outcomes from 3 prospective trials of image-guided PBT for prostate cancer conducted at a single institution. From August 2006-September 2007, 211 patients (low risk n = 89, intermediate risk n = 82, and high-risk n = 40) were enrolled in one of the three trials. Dosages delivered were 78 cobalt gray equivalents (CGE) for low risk and 78 to 82 CGE for intermediate-risk. Participants with high-risk disease received 78 CGE with weekly concomitant chemotherapy, followed by six months of androgen deprivation therapy (ADT). Five-year OS of 93%, 88%, and 86% were reported for low, intermediate, and high-risk patients, respectively. FFBP rates for the same time period were 99% for both low and intermediate risk and 76% for high-risk patients. There was a single instance of acute grade 3 GU toxicity. One acute grade 3 and 2 late grade 3 GI events throughout the entire group resulted in a 5-year incidence of 1%. Limitations to this study include overall study design and lack of a control group. The authors concluded that image-guided PBT was highly effective with minimal toxicities. While outcomes were favorable, the lack of control group limits interpretation of the studies and does not allow assessment of PBT outcomes compared to other forms of radiation therapy.

Yu et al. (2013) conducted a retrospective cohort analysis using data from the Chronic Condition Warehouse, a national database for Medicare fee-for-service claims from patients with specific conditions. The investigators identified patients who were age 66 and older with prostate cancer and treated with IMRT or PBT. To evaluate toxicity, each patient who received PBT was matched with two patients who received IMRT based on similar sociodemographic and clinical characteristics. Toxicity was reported at six months post-treatment and included 421 patients who received PBT matched to 842 patients who received IMRT, and at twelve months post-treatment and included 314 patients who received PBT matched to 628 patients who received IMRT. At six months, GU toxicity was significantly lower in patients who received PBT vs. IMRT (5.9% vs. 9.5%; OR = 0.60, 95% CI = 0.38–0.96, p = 0.03). However, there was no difference at twelve months post-treatment (18.8% vs. 17.5%; OR = 1.08, 95% CI = 0.76–1.54, p = 0.66). At six months and twelve months post-treatment, there was no difference in GI or other toxicities. The authors concluded that in a national sample of Medicare beneficiaries, patient who were treated with IMRT or PBT for prostate cancer had no difference in toxicity rates at twelve months post-treatment, and that additional longitudinal studies evaluating the effectiveness of PBT in comparison to IMRT are needed prior to widespread use of PBT for prostate cancer.

Sheets et al. (2012) evaluated the comparative morbidity and disease control of IMRT, PBT and conformal RT for primary prostate cancer treatment. Main outcomes were rates of GI and GU morbidity, erectile dysfunction, hip fractures and additional cancer therapy. In a comparison between IMRT and conformal RT (n = 12,976), men who received IMRT were less likely to experience GI morbidity and fewer hip fractures, but more likely to experience erectile dysfunction. IMRT patients were also less likely to receive additional cancer therapy. In a comparison between IMRT and PBT (n=1,368), IMRT patients had a lower rate of GI morbidity. There were no significant differences in rates of other morbidities or additional therapies between IMRT and PBT.

Several large population-based cohort studies using Surveillance Epidemiology and End Results (SEER) data, have found greater GI toxicity with PBT than IMRT. Kim et al. (2011) reported that patients treated with RT are more likely to have procedural interventions for GI toxicities than patients with conservative management, and patients treated with PBT therapy experienced greater GI morbidity relative to IMRT patients. The elevated risk persisted beyond 5 years.

To further elucidate the clinical advantages and disadvantages between various types of radiation therapy used in prostate cancer, additional clinical trials are underway (NCT01617161, NCT00969111 and NCT03561220). For more information, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

American Urological Association (AUA)/American Society for Radiation Oncology (ASTRO)

In a 2022 systematic review, the AUA and ASTRO developed a clinical guideline regarding localized prostate cancer. This guideline was endorsed by the Society of Urologic Oncology (SUO). Patients with clinically localized prostate cancer, defined as up to clinical stage T3 prostate cancer without nodal or distant metastasis (N0M0) on conventional imaging, were the target population. The guideline conditionally recommends proton therapy as a treatment option for prostate cancer, but states it has not been found to be superior to other radiation modalities in terms of cancer outcomes or toxicity profile (Eastham et al., 2022).

National Comprehensive Cancer Network (NCCN)

The NCCN Panel believes that photon and PBRT are both effective at achieving highly conformal RT with acceptable and similar biochemical control and long-term side effect profiles. No clear evidence supports a benefit or decrement of one treatment over another. Conventionally fractionated PBT can be considered a reasonable alternative to x-ray-based regimens at clinics with appropriate technology, physics, and clinical expertise (NCCN, 2023).

Skull-Based Tumors

In a Cochrane review, El Sayed et al. (2021) compared the effects and toxicity of proton and photon adjuvant radiation therapy in people with chordoma confirmed by biopsy. The study included six observational studies that were all judged to be at a high risk of bias; four studies were included in the meta-analysis. Adults with pathologically confirmed primary chordoma, irradiated with curative intent, with protons or photons, in the form of fractionated RT, SRS, SBRT or IMRT were included. The primary outcomes were local control, mortality, recurrence, and treatment-related toxicity. The authors concluded there was very low-certainty evidence to show an advantage for proton therapy in comparison to photon therapy with respect to local control, mortality, recurrence, and treatment related toxicity. The authors note that as radiation techniques evolve, multi-institutional data should be collected prospectively and published, to help identify patients that would most benefit from the available radiation treatment techniques. Limitations include a non-randomized design and small sample sizes.

Lee et al. (2021) conducted a systematic review on proton therapy for patients with nasopharyngeal cancer (NPC), focusing on the toxicity endpoints. A total of 491 studies were found on the topic (no randomized data), and nine studies were found to have sufficient focus and relevance to be included. NPC patients were examined in all nine retrospective studies, except one, which included paranasal sinus cancer. One study was a reirradiation study. Four studies used 3D or double scatter technique, while all others used intensity-modulated proton therapy. Oncologic outcomes were similar to IMRT rates, with 2-year local and regional PFS ranging from 84% to 100%, 2-year PFS ranging from 75% to 88.9%, and 2-year OS ranging from 88% to 95% in the up-front setting. Four comparison studies with IMRT found significantly lower feeding tube rates (20% versus 65%,, $p = .015$; and 14% versus 85%, $p < .001$) with proton therapy as well as lower mucositis (G2 46% versus 70%, $p = .019$; and G3 11% versus 76%, $p = .0002$). All other acute and late effects were not statistically significant but largely improved with proton therapy. The authors concluded NPC patients maintained good outcomes with improved toxicity profile, likely due to sparing of dose to normal structures when receiving proton therapy. The authors recommend further prospective studies to better quantify the magnitude of benefit. Limitations include small number of studies, short follow-up periods and retrospective study design.

In a Hayes technology assessment for PBT for treatment of chordoma and chondrosarcoma of the skull base, PBT was reported to be relatively safe, with a moderate risk of acute toxicities and a lower risk of long-term complications. The assessment notes that PBT has similar efficacy as photon-based EBRT technologies and may reduce the risk of certain complications in adult patients. Additional well-designed, long-term studies comparing PBT with other therapies is recommended (2019, Updated 2022).

Zhou et al. (2018) performed a meta-analysis to compare the effectiveness of photon therapy, PBT, and carbon ion therapy (CIT) for chordoma. Twenty-five studies were included, with results showing that the 3-, 5-, and 10-year OS rates were higher for stereotactic RT (SRT), PBT, and CIT than for conventional RT. The 10-year OS was higher for PBT than for SRT. The analysis revealed that particle therapy was more effective following surgery for chordoma than conventional RT. After ten years, PBT was more beneficial than SRT. However, future studies should include more studies to enable accurate meta-analysis and a better exploration of prognosis.

The use of PBT to treat chondrosarcoma of the skull base after surgery is widely accepted, but studies demonstrating the need for PBT and its superiority in comparison to RT with photons are lacking. In a systematic review, Amichetti et al. (2010) reported that studies of PBT for skull-based chondrosarcoma resulted in LC ranging from 75% to 99% at five years. There were no prospective trials (randomized or non-randomized), but four uncontrolled single-arm studies with 254 patients were included. The authors concluded that PBT following surgical resection showed a very high probability of medium- and long-term cure with a relatively low risk of significant complications.

A systematic review of seven uncontrolled single-arm studies concluded that the use of protons has shown better results in comparison to the use of conventional photon irradiation, resulting in the best long-term (10 years) outcome for skull-based chordomas with relatively few significant complications (Amichetti et al., 2009).

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's model policy states PBT is considered reasonable in instances where sparing the surrounding tissue cannot be adequately achieved with photon-based radiotherapy and is of added clinical benefit to the patient. Disease sites that frequently support the use of PBT include tumors that approach or are located at the base of skull, including chordoma and chondrosarcomas (2017). (Accessed September 13, 2022)

National Comprehensive Cancer Network (NCCN)

NCCN guidelines for bone cancer states that specialized techniques, including particle beam RT with protons, should be considered as indicated in order to allow high-dose therapy while maximizing normal tissue sparing in patients with chondrosarcoma or chordoma. PBT may be considered for patients with good long-term prognosis to better spare uninvolved brain and preserve cognitive function (NCCN, 2023).

NCCN guidelines on HNC state that use of proton therapy is an area of active investigation. In cancers of the oropharynx, nasopharynx, supraglottic larynx, salivary glands, mucosal melanoma, and other primary tumors of the head and neck, proton therapy can be considered when normal tissue constraints cannot be met by photon-based therapy. Additionally, either IMRT or proton therapy is recommended for maxillary sinus or paranasal/ethmoid sinus tumors to minimize dose to critical structures (NCCN, 2022).

Unproven Indications

Quality evidence in peer-reviewed medical literature evaluating proton beam radiation therapy for the following indications is limited. Future robust RCTs are warranted along with long-term outcomes to establish the safety and efficacy of this treatment.

Age-Related Macular Degeneration (AMD)

Evans et al. (2020) updated a previously conducted systematic review (Evans, 2010) that examined the effects of radiotherapy on neovascular AMD. A search was conducted using CENTRAL, MEDLINE, Embase, LILACS and three trials registers for randomized controlled trials in which radiotherapy was compared to another treatment, sham treatment, low dosage irradiation or no treatment in people with choroidal neovascularization (CNV) secondary to AMD. Outcomes included best-corrected visual acuity (BCVA) (loss of three or more lines, change in visual acuity), contrast sensitivity, new vessel growth, QOL and adverse effects at any time point. A total of eighteen studies (n = 2,430 people, 2,432 eyes) were included, and the radiation therapy with dosages ranging from 7.5 to 24 Gy. Three of these studies investigated brachytherapy (plaque and epimacular), the rest were studies of external beam radiotherapy (EBM) including one trial of stereotactic radiotherapy. The authors concluded that the evidence is uncertain regarding the use of radiotherapy for neovascular AMD. They stated that: 1) most studies took place before the routine use of anti-VEGF, and before the development of modern radiotherapy techniques such as stereotactic radiotherapy; 2) visual outcomes with epimacular brachytherapy are likely to be worse, with an increased risk of adverse events,

probably related to vitrectomy; 3) the role of stereotactic radiotherapy combined with anti-VEGF is currently uncertain; and 4) further research on radiotherapy for neovascular AMD may not be justified until current ongoing studies have reported their results.

In a systematic review, Bekkering et al. (2009) evaluated the effects and side effects of PBT for indications of the eye. All studies that included at least ten patients and that assessed the efficacy or safety of PBT for any indication of the eye were included. Five controlled trials, two comparative studies and 30 case series were found, most often reporting on uveal melanoma, choroidal melanoma and AMD. Methodological quality of these studies was poor. Studies were characterized by large differences in radiation techniques applied within the studies, and by variation in patient characteristics within and between studies. Results for uveal melanoma and choroidal melanoma suggest favorable survival, although side effects are significant. Results for choroidal hemangioma and AMD did not reveal beneficial effects from proton radiation. There is limited evidence on the effectiveness and safety of due to the lack of well-designed and well-reported studies.

A RCT by Zambarakji et al. (2006) studied 166 patients with angiographic evidence of classic choroidal neovascularization resulting from AMD and best-corrected visual acuity of 20/320 or better. Patients were assigned randomly (1:1) to receive 16-cobalt gray equivalent (CGE) or 24-CGE PBT in two equal fractions. Complete ophthalmological examinations, color fundus photography, and fluorescein angiography were performed before and three, six, 1twelve, eighteen, and 24 months after treatment. At twelve months after treatment, 36 eyes (42%) and 27 eyes (35%) lost three or more lines of vision in the 16-CGE and 24-CGE groups, respectively. Rates increased to 62% in the 16-CGE group and 53% in the 24-CGE group by 24 months after treatment. Radiation complications developed in 15.7% of patients receiving 16-CGE and 14.8% of patients receiving 24-CGE. The authors concluded that no significant differences in rates of visual loss were found between the two dose groups.

Clinical Practice Guidelines

American Academy of Ophthalmology (AAO)

AAO preferred practice patterns state that RT has insufficient data to demonstrate clinical efficacy and is not recommended in the treatment of AMD (Flaxel et al., 2019).

Bladder Cancer

Takaoka and colleagues (2017) conducted a retrospective review to assess outcomes, prognostic factors and toxicities of PBT as a component of trimodal bladder-preserving therapy for muscle-invasive bladder cancer. Trimodal bladder-preserving therapy consisted of maximal transurethral resection of the bladder tumor, small pelvis (conventional) photon radiation, intra-arterial chemotherapy and PBT. Seventy patients with cT2-3N0M0 muscle-invasive bladder cancer were included who received treatment from 1990 to 2015 at a single institution. The OS and PFS rate, time to progression, predictive factors for progression and toxicities were analyzed. Progression was defined as when muscle-invasive recurrence, distant metastasis or upper urinary tract recurrence was observed. The patients' median age was 65 (range 36-85) years. The median follow-up period was 3.4 years (range 0.6-19.5 years). The 5-year cumulative OS rate, PFS rate and time to progression rate were 82%, 77%, and 82%, respectively. In univariate and multivariate analyses, tumor multiplicity and tumor size (≥ 5 cm) were significant and independent factors associated with progression (hazard ratio 3.5, 95% confidence interval 1.1-12; hazard ratio 5.0, 95% confidence interval 1.3-17; $p < 0.05$ for all). As for toxicity, 26 (18%) patients had grade 3-4 acute hematologic toxicities and two (3%) patients had grade 3 late GU toxicity. No patient had to discontinue the treatment due to acute toxicity. The authors concluded that trimodal therapy including both conventional and proton radiation was well tolerated and may be an effective treatment option for selected muscle-invasive bladder cancer patients. Further studies are needed to determine whether PBT is integral to this multi-modality therapy.

Miyanaga et al. (2000) conducted a small prospective uncontrolled clinical study to assess the efficacy and safety of PBT and/or conventional photon therapy for bladder cancer. The study involved 42 patients who received PBT to the small pelvic space following intra-arterial chemotherapy. At 5-year follow-up, the bladder was preserved in 76% of patients and 65% were free of disease. The disease-specific survival rate was 91%. Patients with large and multiple tumors were more at risk of cancer recurrence than patients with single, small tumors. Nausea and vomiting, irritable bladder and ischialgia were the main side effects.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines do not address the use of PBT for treating bladder cancer (NCCN, 2022).

Brain and Spinal Cord Tumors

Petr et al. (2018) assessed structural and hemodynamic changes of healthy brain tissue in the cerebral hemisphere contralateral to the tumor following conventional (photon) and proton radiation with concurrent chemotherapy. Sixty-seven adult patients diagnosed with glioblastoma undergoing adjuvant conventional (n = 47) or proton (n = 19) radiotherapy with temozolomide after tumor resection underwent T1-weighted and arterial spin labeling magnetic resonance imaging. Changes in volume and perfusion before and 3-6 months after were compared between therapies. A decrease in gray matter (GM) and white matter (WM) volume was observed in patients receiving conventional radiation compared to the pre-RT baseline. In contrast, for the proton therapy group, no significant differences in GM or WM volume were observed. GM volume decreased with 0.9% per 10 Gy dose increase and differed between the radiation modalities. Perfusion decreased in conventional radiation therapy patients, whereas the decrease in proton therapy patients was not statistically significant. There was no correlation between perfusion decrease and either dose or radiation modality. The authors concluded that proton therapy may reduce brain volume loss compared to photon therapy, with decrease in perfusion being comparable for both modalities. As this was an uncontrolled retrospective study with a surrogate end-point (brain volume loss on imaging), prospective randomized trials are needed to compare the effect of proton and conventional radiotherapy (CRT) on imaging and clinical outcomes.

Kabolizadeh et al. (2017) conducted a single-center, retrospective, case series to evaluate local control (LC), OS, disease-specific survival, and distant failure in 40 patients with unresected chordoma and treated with photon/proton radiation therapy. Tumor response was assessed using the modified Response Evaluation Criteria in Solid Tumors (mRECIST). To characterize tumor response the soft tissue and bone compartments of the tumor were defined separately as the soft tissue target volume, bone target volume and combined total target volume. Twenty-seven patients had sacrococcygeal chordoma, and the remaining patients had mobile spine tumors, which included nine cervical, one thoracic, and three lumbar. Thirty-nine patients underwent proton therapy only or predominantly proton therapy mixed with photons to limit the radiation dose to adjacent critical normal structures. Only 4 patients received either concurrent or neoadjuvant systemic treatments. The median age was 67 years (range, 36-94 years) and median follow-up, after completion of radiation therapy, was 50.3 months (range, 2–216.4 months). At 5-years, LC, OS, disease-specific survival, and distant failure were 85.4%, 81.9%, 89.4%, and 20.2%, respectively. Nineteen patients had complete sets of regular imaging scans (a total of 84 CT and MRI scans were reviewed) and of those, only 4 local failures had occurred at 34, 46, 78 and 82 months after treatment. The authors concluded that their results support the use of high-dose definitive radiation therapy in select patients with unresected spine and sacral chordomas, and that soft tissue target volume is the best indicator of tumor response. Limitations of this study include its design, the small number of patients with local failure and limited follow-up periods.

Indelicato et al. (2016) conducted descriptive analysis using data from a single-institution. In this prospective case series study, researchers sought to evaluate the effectiveness of definitive or adjuvant external beam proton therapy in patients with chordomas and chondrosarcomas of the spine. Outcomes of interest included distant metastases (DM), OS, cause-specific survival, local control (LC) and disease-free survival (DFS). A total of 51 patients participated with a median age of 58 years (range, 22-83 years) and median follow-up of 3.7 years (range, 0.3-7.7 years). There were 34 patients with chordomas, and seventeen patients with chondrosarcomas, which were all grade 2 or higher. The anatomic distribution was as follows: sacrum (n = 21), cervical spine (n = 20), and thoracolumbar spine (n = 10). The median dose of radiation therapy was 70.2 Gy (range, 64.2-75.6 Gy). The 4-year LC, freedom from distant metastases, DFS, cause-specific survival, and OS rates were 58%, 86%, 57%, 72%, and 72%, respectively. A total of 25 patients experienced disease recurrence: eighteen local recurrences, six local and distant recurrences, and 1 DM. In patients with a local relapse, the median time to progression was 1.7 years (range, 0.2-6 years). The median survival after local progression was 1.7 years (range, 0.1-4.9 + years). Regression analysis results showed that younger patients had a significantly higher risk for local reoccurrence and that patients whose initial management was only surgery also had a higher rate of reoccurrence however, these patients may represent a high-risk subset. The authors concluded that high-dose proton therapy controls more than half of spinal chordomas and chondrosarcomas and compares favorably with historic photon data. Local progression is the dominant mode of treatment failure, and it may be reduced by treating patients at the time of initial diagnosis. Limitations of this study include its design, small sample size and small number of select events, which may have impacted the statistical validity of the regression analysis results.

Shih et al. (2015) conducted a prospective single arm trial to evaluate potential treatment toxicity and PFS in patients (n = 20) with low-grade glioma who were treated with PBRT. Patients with World Health Organization (WHO) grade 2 glioma who were eligible for radiation therapy were enrolled in the study. All patients received proton therapy at a dose of 54Gy in 30 fractions. Baseline and regular post-treatment evaluations of neuroendocrine function, QOL, and neurocognitive function were performed. PBRT was tolerated without difficulty by all twenty patients. The median follow-up after proton therapy was 5.1 years. Intellectual functioning was within the normal range for the group at baseline, and remained stable over time. Executive functioning, attention/working memory, and visuospatial ability also were within normal limits; however, eight patients had baseline neurocognitive impairments observed in language, memory, and processing speed. There was no overall decline in cognitive functioning over time. New endocrine dysfunction was detected in six patients, and all but one had received direct irradiation of the hypothalamic-pituitary axis. No changes were noted in QOL over time. The PFS rate at three years was 85% but fell to 40% at five years. The authors concluded patients with low-grade glioma tolerate proton therapy well, and a subset develops neuroendocrine deficiencies. Additionally, there was no evidence for overall decline in QOL or cognitive function. The authors recommend larger studies that include the integration of standardized, contemporary chemotherapy regimens with randomization of proton versus photon therapy to characterize potential differences in radiation late effects. Limitations of this study include small sample size, lack of comparative group and randomization.

Noel et al. (2002) conducted a retrospective review of seventeen patients with meningioma to evaluate the efficacy and the tolerance of an escalated dose of external conformal fractionated RT combining photons and protons. Five patients presented a histologically atypical or malignant meningioma, twelve patients had a benign tumor that was recurrent or rapidly progressive. In two cases, RT was administered in the initial course of the disease and in fifteen cases at the time of relapse. A highly conformal approach was used combining high-energy photons and protons for approximately 2/3 and 1/3 of the total dose. The median total dose delivered within gross tumor volume was 61 CGE (25-69). Median follow-up was 37 months (17-60). The 4-year LC and OS rates were 87.5 +/- 12% and 88.9 +/- 11%, respectively. Radiologically, there were eleven stable diseases and 5 partial responses. The authors concluded that in both benign and more aggressive meningiomas, the combination of conformal photons and protons with a dose escalated by 10-15% offers clinical improvements in most patients as well as radiological long-term stabilization. Limitations of this study include small sample size and study design.

Several clinical trials studying PBT in patients with various types of brain tumors are active or recruiting.
For more information, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's guideline regarding radiation therapy for IDH-mutant WHO grade 2 and grade 3 diffuse glioma conditionally recommends proton therapy as an option to reduce acute and late toxicity, especially for tumors located near critical organs at risk (OARs) (Halasz et al., 2022).

National Comprehensive Cancer Network (NCCN)

NCCN guidelines for CNS cancers states that when toxicity is a concern during management of spinal ependymoma or medulloblastoma in adults, PBRT should be considered if available. Highly conformal fractionated RT techniques may be conditionally considered for meningiomas to spare critical structures and uninvolved tissue. Proton therapy for patients with good long-term prognosis to better spare uninvolved brain and preserve cognitive function may be conditionally considered for anaplastic gliomas/glioblastoma high-grade and astrocytoma IDH-Wild Type. Preliminary data suggest that proton therapy could reduce the radiation dose to developing brain tissue and potentially diminish toxicities without compromising disease control (NCCN, 2022).

Breast Cancer

DeCesaris (2019) conducted single-institution, retrospective cohort analysis to evaluate acute skin toxicity, i.e., radiation dermatitis (RD) or skin hyperpigmentation (SH) in patients with primary invasive breast cancer who underwent radiation therapy with either photon or proton radiation therapy. Skin toxicity was recorded using Common Terminology Criteria for Adverse Events version 4.0 criteria and scored by treating physicians on a weekly basis. For each patient, the highest recorded grades of RD and SH were analyzed. A total of 86 patients received treatment with a median age of 53 years (range, 245 – 78 years) and median RT dose of 60 Gy (range, 45 – 70 Gy). Of those, 47 (55%) received photon beam therapy and 39 (45%) received PBT. Patients treated with proton beam radiation therapy had a statistically significant higher rate of grade ≥ 2 RD compared

with patients who were treated with photon radiation therapy (69.2% vs. 29.8%, p < 0.001). There was no difference in the rates of grade 3 RD or SH between the modalities. The authors concluded that women who will be undergoing proton beam radiation therapy should receive counseling regarding its potential for grade ≥ 2 skin toxicities. Limitations of this study include its design, use of subjective assessments, and that during treatment optically stimulated luminescent dosimeters were not used to measure patients' radiation exposure.

Verma et al. (2017) conducted a single-institution retrospective cohort study to evaluate acute toxicity in patients with locally advanced breast cancer and receiving comprehensive regional nodal irradiation (CRNI) with adjuvant PBT from 2011–2016. PBT targeting the intact breast/chest wall and CRNI including the axilla, supraclavicular fossa, and internal mammary lymph nodes consisted of a 3-dimensional uniform scanning technique. In 2016, the institution transitioned to a pencil beam scanning (PBS) technique. The change in technique was driven by anticipated dosimetric advantages including decreased dose to the skin surface and to cardiopulmonary organs, and shorter planning and treatment delivery time. Toxicities were assessed weekly during treatment, one month following treatment completion, and then, every 6 months. A total of 91 patients were treated with a median follow-up period of 15.5 months. The most common toxicities were dermatitis and/or skin infections, but esophagitis and fatigue were also observed. Acute dermatitis of grades 1, 2, and 3 occurred in 23%, 72%, and 5%, respectively. Eight percent (n = 7) required treatment breaks due to dermatitis and the median time to resolution of acute skin toxicity was 32 days. Grades 1, 2, and 3 esophagitis developed in 31%, 33%, and 0%, respectively. The authors concluded that PBT for breast cancer as part of CRNI appears to have toxicity rates comparable to prior published studies e.g., Cuaron et al. (2015) reported 71.4% of those who received PBT developed grade 2 dermatitis however, Bradley et al. (2016) reported 100% developed grade 2 dermatitis. While the use of PBT with CRNI may have dosimetric advantages, particularly to the heart and other OARs, toxicities observed with its use demonstrates the need for randomized controlled trials comparing PBT to other radiation modalities.

Bradley et al. (2016) conducted a prospective case series study to evaluate the clinical feasibility and potential benefits of PBT in breast cancer patients who were at risk for regional nodal disease. In this pilot study, the primary endpoint was cardiac V5, testing the hypothesis that PBT could reduce the volume of the heart receiving 5 Gy by ≥ 50% when compared to CRT. The secondary endpoints included acute toxicity and other dosimetric parameters of target coverage and exposure to at-risk organs. PBT and CRT plans, targeting the regional nodes, were created for each patient. Patients were evaluated weekly while on RT, 4 weeks after RT was completed and at 6-month intervals thereafter. Toxicity was recorded using the Common Terminology Criteria for Adverse Events (CTCAE, v4.0). A total of 18 women enrolled with a median age of 51.8 years (range, 42–73 years) and a median follow-up period of 20 months (range, 2–31 months). Ten of the women received only PBT and 8 received combination therapy of PBT and photon beam RT. All patients had improved heart and lung dose with PBT. The primary endpoint, which was to determine if PBT could reduce cardiac V5 by ≥ 50%, was achieved. Of the nine patients with left-sided breast cancer, the median cardiac dose decreased from 5.9 Gy with CRT to 0.6 Gy with PBT (p = 0.004). In patients with right-sided breast cancer, the median cardiac dose decreased from 2.9 Gy with CRT to 0.5 Gy with PBT (p = 0.004). No patients developed grade 4 + toxicities. Four (22%) patients developed grade 3 dermatitis and of these, 3 were treated with PBT and 1 was treated with combination PBT and CRT. All of the patients developed grade 2 dermatitis, which resolved within 1 month of the completion of therapy. However, 1 patient developed cellulitis and required a course of antibiotics. Additional acute grade 2 toxicities included: fatigue (n = 6), esophagitis (n = 5), nausea (n = 1) and dyspnea (n = 1). The authors acknowledged that their rate of patients with grade 3 acute skin toxicity was not unexpected given the higher skin dose with PBT and concluded that PBT for regional node irradiation after mastectomy or breast conserving surgery offers a lower cardiac dose particularly for patients with left-sided breast cancer and without grade 4 + toxicities. Limitations of this study include its design, small sample size and higher toxicity rates compared with other forms of RT, e.g., intensity modulated RT.

Verma et al. (2016a) performed a systematic review of clinical outcomes and toxicity of PBT for treating breast cancer. Nine original studies were analyzed, however the types of studies and the volume of patients in those studies were not specifically cited by the authors. Conventionally fractionated breast/chest wall PBT produced grade 1 dermatitis rates of approximately 25% and grade 2 dermatitis in 71%-75%. This is comparable or improved over the published rates for photons. The incidence of esophagitis was decreased if the target coverage was compromised in the medial supraclavicular volume, a finding that echoes previous results with photon RT. From the limited available data, the rate of grade 2 esophagitis ranged from 12% to 29%. Using PBT-based accelerated partial breast irradiation (PBI), the rates of seroma/hematoma and fat necrosis were comparable to those reported in the existing data. Radiation pneumonitis (RP) and rib fractures remain rare. PBT offers the potential to minimize the risk of cardiac events, keeping the mean heart dose at ≤ 1 Gy. However, definitive clinical experiences remain sparse. Results from clinical trials in progress, comparing protons to photons, will further aid in providing conclusions. Limitations to this review included a general lack of data and low number of participants in the available studies.

Cuaron et al. (2015) conducted a single-institution case series study to report dosimetry and early toxicity data in patients with breast cancer. Retrospectively collected data from consecutive patients diagnosed with non-metastatic breast cancer, no prior history of chest wall radiation and treated with PBT postoperatively were studied. Patients with unfavorable cardiopulmonary anatomy were usually referred to this institution. Post-lumpectomy patients with large breast size were not offered treatment due to a higher propensity for day-to-day measurement differences in the target position. Patients were evaluated weekly while on RT, 4 weeks after RT was completed, and at 12–24-week intervals thereafter. Toxicity was recorded using the Common Terminology Criteria for Adverse Events (CTCAE, v4.0). A total of 30 women were included in the study with a median age of 49 years (range, 29–86 years), cancer staging was as follows: eight had stage II, twenty had stage III and two had chest wall recurrence. The median follow-up was 9.3 months (range, 2.3–18.6 months). With PBT, full coverage of the planned target value was achieved, and it significantly spared the heart, lungs and contralateral breast. Of those with greater than 3 months of follow-up (n = 28), 71.4% developed grade 2 dermatitis and of those, 28.6% experienced moist desquamation. Eight (28.6%) developed grade 2 esophagitis and one developed grade 3 reconstructive complications. The authors concluded that in this series of 30 patients, PBT achieved excellent coverage of the target volume while sparing the heart, lungs, and contralateral breast, that the treatment was well tolerated, and that additional studies assessing long-term outcomes and toxicity are needed. Limitations of this study include its design, exclusion of women with large breast size, and higher toxicity rates compared with other forms of RT, e.g., intensity modulated RT.

Bush et al. (2014) performed a single center study of 100 subjects who received postoperative PBI using PBT after undergoing partial mastectomy with negative margins and axillary lymph nodes. After following these individuals for an average of five years, the researchers concluded that ipsilateral recurrence-free survival with minimal toxicity was excellent. While the authors acknowledged that cosmetic results may be improved with PBT over those reported with photon-based techniques, there was nothing in the study demonstrating that PBT outcomes were superior to the current standard of care.

To further elucidate the clinical advantages and disadvantages between PBT and other types of radiation therapy used in breast cancer, additional clinical trials are underway, NCT02603341, NCT01245712, and NCT03391388, go to https://clinicaltrials.gov/. (Accessed September 13, 2022).

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines do not address the use of PBT for treating breast cancer (NCCN, 2022).

Choroidal Hemangiomas

Mathis et al. (2021) conducted a retrospective multi-center study that compared the functional and anatomical effectiveness of PBT versus photodynamic therapy (PDT) in a real-life setting for the treatment of circumscribed choroidal hemangioma. The study included a total of 191 patients with a diagnosis of choroidal hemangioma, 119 patients (62.3%) were treated by PDT and 72 patients treated by PBT. The final best-corrected visual acuity did not differ significantly between the two groups ($p = 0.932$) and final thickness was lower in the PBT compared with the PDT group ($p = 0.001$). Fifty-three patients (44.5%) initially treated by PDT required at least one other therapy and were associated with worse final best-corrected visual acuity ($p = 0.037$). None of the patients treated by PBT needed second-line therapy. In multivariate analysis, only an initial thickness greater than 3 mm remained significant ($p = 0.01$) to predict PDT failure. The authors concluded PDT and PBT have similar functional and anatomical outcomes for circumscribed choroidal hemangioma ≤ 3 mm; although PDT sometimes requires multiple sessions. Additionally, for tumors > 3mm, PBT seems preferable as it can treat the tumor in one session with better anatomical and functional outcomes. The authors recommended further large-scale studies to better define a thickness threshold above which PDT is less efficient. Limitations include the retrospective nature of the study, lack of randomization and small study size.

Hocht et al. (2006) conducted a single-center, retrospective study of 44 consecutive patients with choroid hemangiomas treated with photon therapy (n = 19) or proton therapy (n = 25). Outcomes were measured by visual acuity, tumor thickness, resolution of retinal detachment, and post-treatment complications. Mean follow-up was 38.9 months and 26.3 months, and median follow-up was 29 months and 23.7 months for photon and proton patients, respectively. Tumor thickness was greater in the photon group than in the proton group. In the collective groups, 91% were treated successfully, and there was no significant difference in the outcomes between the two groups. The authors concluded that RT is effective in treating choroidal hemangiomas with respect to visual acuity and tumor thickness, but a benefit of proton versus photon therapy could not be detected.

Three additional studies showed some improvement in tumor regression and visual acuity following PBT; however, these studies were small and retrospective in nature (Chan et al., 2010; Levy-Gabriel et al., 2009; Frau et al., 2004).

Gastrointestinal (GI) Cancers

Fok et al. (2021) conducted a systematic review and meta-analysis that compares dosimetric irradiation of OARs and oncological outcomes for PBT versus conventional photon-based radiotherapy in locally advanced rectal cancer. Eight articles with a total of 127 patients met the inclusion criteria. There was significantly less irradiated small bowel with PBT compared to 3DCRT and IMRT (MD -17.01, CI [-24.06, – 9.96], $p < 0.00001$ and MD -6.96, CI [-12.99, – 0.94], $p = 0.02$, respectively). Similar dosimetric results were observed for bladder and pelvic bone marrow. Three studies reported clinical and oncological results for PBT in recurrent rectal cancer with overall survival reported as 43 %, 68 % and 77.2 %, and one study in primary rectal cancer with 100 % disease free survival. The authors concluded PBT treatment plans resulted significantly less irradiation of OARs for rectal cancer when compared to conventional photon-based radiation therapy. The authors note there are currently no ongoing clinical trials for primary rectal cancer and PBT and more research is required to validated PBTs role in organ preservation without increasing toxicity, complete response rate, and dose escalation. Limitations include small sample size and lack of RCTs.

Verma et al. (2016b) conducted a systematic review to identify studies on PBT and gastrointestinal malignancies. The search included PubMed, EMBASE, and abstracts from meetings of the American Society for Radiation Oncology, Particle Therapy Co-Operative Group, and American Society of Clinical Oncology. A total of 39 original investigations were analyzed. For esophageal cancer, twelve studies were analyzed and several of those reported that PBT resulted in a significant dose reduction to intrathoracic OARs and is associated with reduced toxicity, postoperative complications (POCs) while achieving comparable local control and overall survival. However, for some of the studies, contemporaneous comparison groups were lacking, or comparisons were made between PBT and x-ray radiotherapy (XRT), which consisted of either 3D-CRT or IMRT rather than IMRT only. For pancreatic cancer, 5 studies were analyzed. Survival for resected/unresected cases was similar to existing data where IMRT was used and nausea/emesis were numerically lower than what had been reported among patients who received IMRT however, direct head-to-head comparisons were not made. For hepatocellular carcinoma, ten studies were analyzed, and these had the strongest evidence to support use of PBT. Those studies reported very low toxicities, and a phase III trial comparing PBT to TACE showed a trend toward better LC and PFS with PBT. For cholangiocarcinoma, liver metastases, and retroperitoneal sarcoma, survival and toxicity data is comparable to historical photon controls, and stomach and biliary system/gallbladder cancer studies consisted of case reports and small cohort experiences. The authors concluded that PBT offers the potential of lower toxicities without compromising survival or local control. However, there was limited high quality evidence for select gastrointestinal malignancies and that multi-institution, randomized controlled trials are needed.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines do not address PBT in the treatment of gastric cancers (NCCN, 2022).

Esophageal Cancer

A Hayes Health Technology Assessment (2022) for the use of PBT in adults with esophageal adenocarcinoma as an adjunct to chemotherapy and surgery states PBT may have effectiveness that is comparable to both IMRT and 3DCRT and results in significantly lower radiation exposure to nearby OARs, with possibly fewer complications in those undergoing esophagectomy. However, the statistical significance of those findings were mixed. PBT and IMRT were found to have similar rates of nonoperative complications. The overall quality of the body of evidence for PBT for the treatment of esophageal adenocarcinoma was rated as low due to limitations of the individual studies, diverse treatment protocols, and scarcity of evidence for efficacy beyond three years.

Lin et al. (2020) conducted a phase IIB RCT that compared total toxicity burden (TTB) and PFS between IMRT and PBT. Patients were randomly assigned to PBT or IMRT (50.4 Gy) ranked for histology, resectability, induction chemotherapy, and stage. TTB, included a composite score of eleven AEs, including common toxicities as well as POCs in operated patients. The trial began in April 2012 and was approved for closure and analysis upon activation of NRG-GI006 in March 2019, which occurred immediately prior to the planned 67% interim analysis. One-hundred and seven patients (61 IMRT, 46 PBT) of the 145 randomly assigned patients (72 IMRT, 73 PBT), were evaluable. Median follow-up was 44.1 months. Fifty-one patients (30 IMRT, 21 PBT) underwent esophagectomy; 80% of PBT was passive scattering. The posterior mean TTB was 2.3 times higher for

IMRT (39.9; 95% highest posterior density interval, 26.2-54.9) than PBT (17.4; 10.5-25.0). The mean POC score was 7.6 times higher for IMRT (19.1; 7.3-32.3) versus PBT (2.5; 0.3-5.2). The posterior probability that mean TTB was lower for PBT compared with IMRT was 0.9989, which exceeded the trial's stopping boundary of 0.9942 at the 67% interim analysis. The 3-year PFS rate (50.8% v 51.2%) and 3-year overall survival rates (44.5% v 44.5%) were similar. The authors concluded for locally advanced esophageal cancer, PBT reduced the risk and severity of AEs compared with IMRT while maintaining similar PFS. Limitations include small sample sizes, open-label, non-blinding, and single institution design.

Lin et al. (2017) conducted a multi-center retrospective cohort study of patients diagnosed with EC and treated with neoadjuvant chemoradiation. The purpose of this study was to assess the association between RT modality and postoperative outcomes. The outcomes included pulmonary, cardiac and wound complications, and length of stay (LOS), readmission and mortality. A total of 580 EC patients were included and of these, 214 (37%) received 3D-CRT, 255 (44%) received IMRT and 111 (19%) receive PBT. IMRT and PBT were associated with a reduced risk of pulmonary complications compared with 3D-CRT ($p = .001$), and PBT was trending toward being better than IMRT (OR 0.584, $p = .077$). Both IMRT and PBT were associated with a reduced risk of cardiac complications as were older age and history of coronary artery bypass grafting or atrial fibrillation. PBT was associated with a reduced risk of wound complications (OR 0.255, $p = 0.006$, PBT vs. 3D-CRT; OR 0.276, $p = 0.009$, PBT vs. IMRT) yet there was no difference between IMRT and 3D-CRT. Mean LOS was significantly associated with RT modality (13.2 days for 3D-CRT, 11.6 days for IMRT and 9.3 days for PBT ($p < 0.0001$). There was no difference in 60-day readmission rates or deaths during the same hospitalization, or 30, 60 or 90-day postoperative mortality. The authors concluded that IMRT and PBT were associated with significantly reduced rates of POCs compared to 3D-CRT, that these results may show an advantage of PBT over IMRT however, prospective randomized clinical trials will better establish the role of PBT in EC.

Xi et al. (2017) conducted a single-center retrospective cohort study to evaluate outcomes of patients diagnosed with esophageal cancer (EC) and treated with PBT or IMRT. Outcomes included treatment-related toxicity, OS, PFS, locoregional failure-free survival (LRFFS) and distant metastasis-free survival (DMFS). Patients were followed every three months for the first year after radiation therapy, every six months for the following 2 years and then yearly until five years. A total of 343 patients were included and of those ,211 received IMRT and 132 received PBT. The median follow-up period for the IMRT group was 65.1 months (range, 19.4-115.3) and for the PBT group was 44.8 months (range, 11.9 – 110.3 months). The median radiation dose was 50.4 Gy in both the IMRT and PBT groups (ranges, 41.4-66.0 Gy and 45.0-63.0 Gy, respectively). There was no difference in treatment-related toxicities between the groups. The PBT group had better OS ($p = .011$), PFS ($p = .001$), and DMFS ($p = .031$) compared with the IMRT group. In subset analyses, patients with stage I/II disease had no differences in survival. In patients with stage III disease, those who received PBT had higher rates of OS (34.6% vs. 25.0%, $p = .038$) and PFS (33.5% vs. 13.2%, $p = .005$). The authors concluded that PBT was associated with improved OS, PFS and LRFFS, particularly in EC patients with advanced disease and that their results may suggest a benefit of PBT over IMRT. Limitations of this study include its design, that the type of radiation therapy each patient received was based on the multidisciplinary team and the patients' intent rather than randomization, there were differences in patient demographics and baseline characteristics between the groups, and that for some patients, accurate long-term documentation was lacking. Prospective, randomized controlled studies are needed to clarify the role of PBT in EC.

In a retrospective analysis, Wang et al. (2013a) reported that advanced radiation technologies such as IMRT or PBT significantly reduced postoperative pulmonary and GI complication rates compared to 3D-CRT in EC patients. These results need to be confirmed in prospective studies.

Mizumoto et al. (2011) evaluated the efficacy and safety of hyperfractionated concomitant boost PBT in nineteen patients with esophageal cancer. The overall 1- and 5-year actuarial survival rates for all nineteen patients were 79% and 42.8%, respectively. The median survival time was 31.5 months. Of the nineteen patients, seventeen (89%) showed a complete response within four months after completing treatment and two (11%) showed a partial response, giving a response rate of 100% (19/19). The 1- and 5-year LC rates for all nineteen patients were 93.8% and 84.4%, respectively. The results suggest that hyperfractionated PBT is safe and effective for patients with esophageal cancer. Further studies are needed to establish the appropriate role and treatment schedule for use of PBT for esophageal cancer.

Mizumoto et al. (2010) evaluated the efficacy and safety of PBT for locoregionally advanced esophageal cancer. Fifty-one patients were treated using PBT with or without X-rays. All but one had squamous cell carcinoma. Of the 51 patients, 33 received combinations of X-rays and protons as a boost. The other eighteen patients received PBT alone. The overall 5-year actuarial survival rate for the 51 patients was 21.1% and the median survival time was 20.5 months. Of the 51 patients, 40 (78%) showed a complete response within four months after completing treatment and seven (14%) showed a partial response, giving

a response rate of 92% (47/51). The 5-year LC rate for all 51 patients was 38% and the median LC time was 25.5 months. The authors concluded that these results suggest that PBT is an effective treatment for patients with locally advanced esophageal cancer. Further studies are required to determine the optimal total dose, fractionation schedules and best combination of proton therapy with chemotherapy.

An ongoing phase III study is recruiting patients to compare the use of PBT to photon therapy in EC patients (Clinical Trial ID: NCT03801876). For more information, go to http://www.clinicaltrials.gov/. (Accessed September 13, 2022).

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines state that PBT is appropriate when treating esophageal and esophagogastric junction cancers in settings where dose reduction to OARs is necessary and cannot be achieved by 3D-CRT. Because data is early and evolving, patients should receive PBT within a clinical trial (NCCN, 2022).

Gynecologic Cancers

The efficacy of PBT combined with photon radiation for the treatment of cervical cancer was investigated in a prospective uncontrolled study involving 25 patients (Kagei et al., 2003). In this study, 5-year and 10-year survival rates were similar to conventional therapies as reported in the literature. The 10-year survival rate was higher for patients with low stage (89%) compared with advanced stages (40%) of cervical cancer. The treatment caused severe late complications in 4% of patients.

Several clinical trials are recruiting or in progress studying the use of PBT in multiple types of gynecologic cancer (e.g., cervical, ovarian, and uterine). For more information, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines do not address the use of PBT when treating any type of gynecologic cancer (i.e., Cervical Cancer (NCCN, 2022), Ovarian Cancer (NCCN, 2022), Uterine Neoplasms (NCCN, 2022) or Vulvar Cancer (NCCN, 2022).

Head and Neck Cancers (HNC) Not Listed in the Coverage Rationale as Proven

A 2019 Hayes report, Proton Beam Therapy for Treatment of Head and Neck Cancer, assessed multiple clinical studies evaluating the efficacy and safety of PBT in patients with HNC. The majority of the evidence included retrospective studies, data analyses, and systematic reviews. They noted there was some overlap of investigators and, possibly, overlap of patient groups as well. The report concludes that the study abstracts present conflicting findings regarding the use of PBT for treatment of HNC. (Updated 2021).

Seeking to improve LC rate and reduce late AEs, Takayama et al. (2016) evaluated therapeutic results and toxicities of PBT combined with selective intra-arterial infusion chemotherapy (PBT-IACT) in patients with stage III-IVB squamous cell carcinoma of the tongue. Between February 2009 and September 2012, 33 patients were enrolled. After two systemic chemotherapy courses and whole-neck irradiation (36 Gy in 20 fractions), participants were administered concurrent chemoradiotherapy comprising PBT for the primary tumor and the metastatic neck lymph node with weekly retrograde IACT of cisplatin with sodium thiosulfate by continuous infusion. The median follow-up duration was 43 months. The 3-year OS, PFS, LC rate, and regional control rate for the neck were 87%, 74.1%, 86.6%, and 83.9%, respectively. Major acute toxicities > grade 3 included mucositis in 26 cases (79%), neutropenia in seventeen cases (51%), and dermatitis in 11 cases (33%). Late grade 2 osteoradionecrosis was observed in 1 case (3%). The authors concluded that PBT-IACT for stage III-IVB tongue cancer has an acceptable toxicity profile and showed good treatment results, and that this protocol should be considered as a treatment option for locally advanced tongue cancer. This study is limited by the lack of data comparing toxicity to conventional radiation therapy.

Clinical Practice Guidelines

American College of Radiology (ACR)/American Society for Radiation Oncology (ASTRO)

Regarding head and neck tumors, the ACR/ASTRO practice parameter states that PBRT reduces the dose delivered to critical normal structures in the head and neck region that may impact QOL, including optic nerves, optic chiasm, pituitary gland, brain,

brainstem, spinal cord, salivary glands, pharyngeal constrictor muscles, oral cavity, and the emetogenic sites in the posterior fossa (2018).

National Comprehensive Cancer Network (NCCN)

NCCN's HNCs guideline makes no mention of proton beam radiation therapy for cancer of the lip (mucosa), oral cavity, hypopharynx or glottic larynx. The guideline states that use of proton therapy is an active area of investigation, and that proton therapy may be considered when normal tissue constraints cannot be met by photon-based therapy in cancers of the oropharynx, nasopharynx, supraglottic larynx, and salivary glands, as well as mucosal melanoma and other primary tumors of the head and neck. Either IMRT or proton therapy is recommended for maxillary sinus or paranasal/ethmoid sinus tumors to minimize the dose to critical structures (NCCN, 2022).

Lung Cancer

Liao et al. (2018) conducted a single-center randomized trial that compared outcomes of passive scattering proton therapy (PSPT) versus IMRT, both with concurrent chemotherapy, for inoperable NSCLC. The primary end point was the first occurrence of severe (grade ≥ 3) radiation pneumonitis (RP) or local failure (LF). Eligible patients had stage IIB to IIIB NSCLC (or stage IV NSCLC with a single brain metastasis or recurrent lung or mediastinal disease after surgery) and were candidates for concurrent chemoradiation therapy. Pairs of treatment plans for IMRT and PSPT were created for each patient. Patients were eligible for random assignment only if both plans satisfied the same prespecified dose-volume constraints for at-risk organs at the same tumor dose. Compared with IMRT (n = 92), PSPT (n = 57) exposed less lung tissue to doses of 5 to 10 Gy (RBE), which is the absorbed Gy dose multiplied by the relative biologic effectiveness (RBE) factor for protons; exposed more lung tissue to ≥ 20 Gy (RBE) but exposed less heart tissue at all dose levels between 5 and 80 Gy (RBE). The grade ≥ 3 RP was greater for PSPT than IMRT (6.5% for IMRT and 10.5% for PSPT) though the difference did not reach statistical significance; there was no difference observed in LF (10.9% and 10.5% for IMRT and PSPT, respectively). Exploratory analysis showed that the RP and LF rates at twelve months for patients enrolled before versus after the trial midpoint were 21.1% (before) versus 18.2% (after) for the IMRT group and 31.0% (before) versus 13.1% (after) for the PSPT group suggesting that that outcomes for proton therapy improved over the course of the trial as the investigators gained experience. The authors stated that findings from 2 ongoing trials (NCT01993810 and NCT01629498) will provide additional evidence of the efficacy of proton and photon therapies.

Chang et al. (2017) reported 5-year results of a prospective phase II single-institution study evaluating chemotherapy with concurrent high dose PBT in 64 patients with unresectable phase III NSCLC. 5-year OS, PFS, actuarial distant metastases and locoregional recurrence were 29%, 22%, 54%, and 28%, respectively. Acute and late toxic effects with PBT (compared to historical studies with 3D-CRT and/or IMRT) with chemotherapy were very promising. The authors concluded that the study demonstrated that concurrent PBT and chemotherapy was safe and effective in the long term, and that further prospective studies are warranted.

Chi et al. (2017) conducted a systematic review and meta-analysis to assess hypo-fractionated PBT's efficacy relative to that of photon SBRT for early-stage NSCLC. Seventy-two SBRT studies and 9 hypo-fractionated PBT studies (mostly single-arm) were included. PBT was associated with improved OS and PFS in the univariate meta-analysis. The OS benefit did not reach its statistical significance after inclusion of operability into the final multivariate meta-analysis, while the 3-year LC still favored PBT. Researchers concluded that although hypo-fractionated PBT may lead to additional clinical benefit when compared with photon SBRT, no statistically significant survival benefit from PBT over photon SBRT was observed in the treatment of early-stage NSCLC.

Harada et al. (2016) conducted a single-institutional, open label, dose escalation phase I trial to determine the recommended dose of PBT for inoperable stage III NSCLC. Two prescribed doses of PBT were tested: 66 Gy RBE in 33 fractions and 74 Gy RBE in 37 fractions in arms one and two, respectively. The planning target volume included the primary tumor and metastatic lymph nodes with adequate margins. Concurrent chemotherapy included intravenous cisplatin (60 mg/m (2), day 1) and oral S-1 (80, 100 or 120 mg based on body surface area, days 1-14), repeated as four cycles every four weeks. Dose-limiting toxicity (DLT) was defined as grade 3 (severe) toxicities related to PBT during days 1-90. Each dose level was performed in three patients, and then escalated to the next level if no DLT occurred. When one patient developed a DLT, three additional patients were enrolled. Overall, nine patients were enrolled, including 6 in Arm 1 and 3 in Arm 2. The median follow-up time was 43 months, and the median PFS was 15 months. In Arm 1, grade 3 infection occurred in 1 of 6 patients, but no other DLT was reported. Similarly, no DLT occurred in Arm 2. However, one patient in Arm 2 developed grade 3 esophageal fistula at nine

months after the initiation of PBT. From a clinical perspective, the authors concluded that 66 Gy RBE is the recommended dose.

Oshiro et al. (2014) initiated a phase II study to evaluate the safety and efficacy of high-dose PBT with concurrent chemotherapy for unresectable or medically inoperable advanced NSCLC. Patients (n = 15) were treated with PBT and chemotherapy with monthly cisplatin (on Day one) and vinorelbine (on Days one and eight). The treatment doses were 74 Gy RBE for the primary site and 66 Gy RBE for the lymph nodes without elective lymph nodes. The median follow-up period was 21.7 months. None of the patients experienced Grade 4 or 5 non-hematologic toxicities. Acute pneumonitis was observed in three patients (Grade 1 in one, and Grade 3 in two), but Grade 3 pneumonitis was considered to be non-proton-related. Grade 3 acute esophagitis and dermatitis were observed in one and two patients, respectively. Severe (≥ Grade 3) leukocytopenia, neutropenia and thrombocytopenia were observed in ten, seven, and one patients, respectively. Late RP (grades 2 and 3) was observed in one patient each. Six patients (40%) experienced local recurrence at the primary site and were treated with 74 Gy RBE. Disease progression was observed in eleven patients, with the mean survival time being 26.7 months. The authors cited short follow up period as a limitation to this study. They concluded that high-dose PBT with concurrent chemotherapy is safe and useful in the multimodality therapy for unresectable NSCLC.

Sejpal et al. (2011) conducted a single-center, retrospective case series study to evaluate the use of PBT plus concurrent chemotherapy in patients with SNCLC. Outcomes included acute and subacute toxicity and were evaluated using Common Terminology Criteria (version 3.0) at least weekly during treatment, at four to six weeks after treatment, every three months for two years and then, every six months. Survival, time to progression and failure patterns were also collected. Comparisons between other radiation treatment modalities (IMRT and 3D-CRT, each with concurrent chemotherapy) were made using historical controls from the same center. A total of 202 patients were included in the analysis: 74 received 3D-CRT, 66 IMRT and 62 PBT. Median follow-up periods were 17.9 months (3D-CRT), 17.4 months (IMRT) and 15.2 months (proton). Median total radiation dose was higher in the PBT group at 74 Gy versus 63 Gy for the other groups. Despite the higher radiation dose in the PBT group, rates of severe (grade ≥ 3) pneumonitis and esophagitis were lower (2% and 5%, respectively) compared with the other groups (3D-CRT, 30% and 18%; IMRT, 9% and 44%, respectively). Due to the short follow-up periods, tumor control and survival were not reported. The authors concluded that in this early and promising study, higher doses of PBT could be delivered to lung tumors with a lower risk of esophagitis and pneumonitis, and that additional clinical trials may further clarify the benefits and risks of PBT in patients diagnosed with SNCLC.

Pijls-Johannesma et al. (2010) conducted a systematic review to test the theory that RT with beams of protons and heavier charged particles (e.g., carbon ions) leads to superior results, compared with photon beams. The authors searched for clinical evidence to justify implementation of particle therapy as standard treatment in lung cancer. Eleven studies, all dealing with NSCLC, mainly stage I, were identified. No phase III trials were found. For PBT, 2- to 5-year LC rates varied in the range of 57%-87%. The 2- and 5-year OS and 2- and 5-year cause-specific survival rates were 31%-74% and 23% and 58%-86% and 46%, respectively. RP was observed in about 10% of patients. For CIT, the overall LC rate was 77%, but it was 95% when using a hypofractionated radiation schedule. The 5-year OS and cause-specific survival rates were 42% and 60%, respectively. Slightly better results (at 50% and 76%, respectively) were reported when using hypofractionation. The results with protons and heavier charged particles are promising. However, the current lack of evidence on the clinical effectiveness of particle therapy emphasizes the need to further investigate the efficiency of particle therapy. The authors concluded that until these results are available for lung cancer, CPT should be considered experimental.

A phase III RCT comparing photon to proton chemoradiotherapy for patients with inoperable NSCLC (NCT01993810) is in progress. For more information, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

American College of Radiology (ACR)

ACR appropriateness criteria addressing nonsurgical treatment for locally advanced NSCLC states that while PBT may have the potential to spare critical normal tissues, more prospective studies are needed (Chang, et al., 2014).

National Comprehensive Cancer Network (NCCN)

NCCN guidelines state that advanced technologies such as PBT are appropriate when needed to deliver curative RT safely when treating NSCLC (NCCN, 2022) and may be appropriate to limit normal tissue toxicity in the treatment of small cell lung cancer (NCCN, 2023).

Lymphomas

Multiple small, lower quality studies have been published on the management of lymphomas with PBT, particularly focused on long term radiation toxicity (König et al., 2019; Horn et al., 2016; Sachsman et al., 2015; Hoppe et al., 2012). Early outcomes are encouraging, but larger prospective studies are needed to confirm long term efficacy.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines for Hodgkin, B-cell, and T-cell lymphomas state that PBT may be appropriate, depending on clinical circumstances. It also states that advanced RT technologies, such as PBT, may offer significant and clinically relevant advantages in specific instances to spare important OARs and decrease the risk for late, normal tissue damage while still achieving the primary goal of LC. NCCN is silent on the use of PBT in the treatment of primary cutaneous lymphoma (NCCN, 2022-2023).

Pancreatic Cancer

There is a lack of robust clinical evidence evaluating PBT for treating pancreatic cancer although research continues (Kim et al., 2018, Hong et al., 2014; Terashima et al., 2012; Hong et al., 2011). Further larger scaled prospective studies are warranted to determine the long-term safety and efficacy of this treatment modality.

Numerous clinical trials are currently in progress studying the use of PBT in multiple types of GI cancer (e.g., esophageal, pancreatic, and retroperitoneal sarcoma). For more information, go to www.clinicaltrials.gov. (Accessed September 13, 2022)

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

NCCN guidelines do not address PBT in the treatment of pancreatic adenocarcinoma (NCCN, 2022).

Vestibular Tumors

In a critical review, Murphy and Suh (2011) summarized the radiotherapeutic options for treating vestibular schwannomas, including single-session stereotactic radiosurgery, fractionated conventional RT, fractionated stereotactic RT and PBT. The comparisons of the various modalities have been based on single-institution experiences, which have shown excellent tumor control rates of 91-100%. Early experience using PBT for treating vestibular schwannomas demonstrated LC rates of 84-100% but disappointing hearing preservation rates of 33-42%. The authors report that mixed data regarding the ideal hearing preservation therapy, inherent biases in patient selection and differences in outcome analysis have made comparison across radiotherapeutic modalities difficult.

The efficacy of PBT for the treatment of tumors of the vestibular system was assessed in two prospective uncontrolled studies involving 30 patients with acoustic neuromas (Bush et al., 2002) and 68 patients with vestibular schwannomas (Harsh et al., 2002). Fractionated PBT effectively controlled tumor growth in all patients with acoustic neuroma, and 37.5% of patients experienced tumor regression. Hearing was preserved in 31% of patients. The actuarial 5-year tumor control rate for patients with vestibular schwannomas was 84%; 54.7% of tumors regressed, 39.1% remained unchanged, and 3 tumors enlarged. The procedure caused some serious side effects in patients with vestibular schwannoma (severe facial weakness), but most side effects were either transient or could be successfully treated.

Clinical Practice Guidelines

Congress of Neurological Surgeons (CNS)

CNS developed an evidence-based guideline on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas. CNS notes that no studies that compare two or all three modalities (Gamma Knife versus LINAC-based radiosurgery versus proton beam) were identified, therefore, no recommendations on outcome could be made (Germano et al., 2018). Combined Therapies

No evidence was identified in the clinical literature supporting the combined use of PBT and IMRT in a single treatment plan.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Radiation therapy is a procedure and, therefore, is not subject to FDA regulation. However, the accelerators and other equipment used to generate and deliver PBRT are regulated by the FDA. Refer to the following website for more information (use product code LHN): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed September 13, 2022)

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Policy History/Revision Information

Date	Summary of Changes
10/01/2023	**Application** ***Individual Exchange Plans*** • Removed language indicating this Medical Policy does not apply to Individual Exchange benefit plans in the states of Massachusetts, Nevada, and New York **Supporting Information** • Archived previous policy version 2023T0132EE

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

EXHIBIT E

CLAIM FORM

Weissman v. UnitedHealthcare Ins. Co. Class Action Settlement
United States District Court for the District of Massachusetts
Case No. 1:19-cv-10580

You MUST sign and return this Claim Form by _____ if you wish to receive payment as part of this settlement. You may also download a copy of this Claim Form at www._____.com.

To receive a payment of up to $75,000, you need to correctly and timely submit this Claim Form and provide documentation that you paid amounts and/or incurred debt for Proton Beam Therapy treatment.

Submit Your Completed Claim Form in Any of the Following Ways:

(1) Email to: _____@_____.com

(2) Mail to: _____
P.O. Box _____
_____, __ _____

(3) Upload at: www._____,com

To be valid, the Claim Form **MUST** be signed and dated, and postmarked, emailed, or uploaded by _____.

PLEASE REVIEW THE INSTRUCTIONS BELOW TO FILE YOUR CLAIM FOR UP TO $75,000 FOR PBRT TREATMENT COSTS

Settlement Class Members may be eligible to receive a settlement payment of up to $75,000 to reimburse them for out-of-pocket costs expended or incurred for PBRT treatment.

In order to make a claim for a settlement payment please provide a response to **Part A** below by stating (1) the total amount paid for Proton Beam Therapy treatment, and (2) the additional amount, if any, you still owe to the medical provider or facility for obtaining Proton Beam Therapy treatment.

You must also provide proof of payment and/or proof of any additional amounts you still owe with this Claim Form. **Part B** describes the documents to provide to show your proof of payment or proof of what you owe with this Claim Form. **Part C** is an *optional* notarized affidavit or sworn statement from you (or an authorized representative) further supporting your claim for the amount you identified.

PLEASE MAKE SURE TO SIGN AND PROVIDE YOUR CONTACT INFORMATION AT THE END OF THIS DOCUMENT.

Part A

I affirm under the penalty of perjury, that to the best of my knowledge, the total amount paid and/or the total amount still owed for Proton Beam Therapy treatment is:

Total Amount Paid: $_____

And, if applicable,

Total Amount Still Owed: $_____

Part B

Please provide copies of any documentation with this completed Claim Form that supports the amount you identified in Response to Part A above.

- Proof of payment includes, but is not limited to: receipt(s) showing payment for Proton Beam Therapy treatment from a hospital, treatment center, or physician; cancelled checks; credit card records; or any other proof of payment for Proton Beam Therapy treatment, including documentation from UnitedHealthcare Insurance Co.

- Proof of What you Owe includes, but is not limited to, loan documentation; current collection notices; unpaid and currently owing invoices or bills from the medical provider or facility; or existing self-pay agreements with a medical care provider that administered Proton Beam Therapy treatment.

Part C

In addition to the information required by Part A and Part B above, you also may provide an **optional statement** from you (or your authorized representative) supporting your claim that the amount identified in Response to Part A above was paid or is still owed as debt. It is not necessary to provide this statement, but it may be helpful. **If you do provide this statement, then it must be notarized.** If you need more room, please attach additional sheets as necessary:

I affirm under penalty of perjury that the responses and/or explanations I have provided above are true and correct, to the best of my knowledge, information, and memory. I also attest that I am legally authorized to submit this form (as a Settlement Class Member or as a spouse, adult child, representative, person with valid durable power of attorney, heir, or responsible family member of a Settlement Class Member).

Signature: _____ Date: _____

Printed Name: _____

Your contact information:

Mailing address: _____

Email Address(es) _____

Phone Number(s): _____

PLEASE NOTE; It is your responsibility to notify the Claims Administrator (Rust Consulting) and Class Counsel if you change your mailing address or other contact information.

If the addressee(s) of this Claim Form is/are unable to fill it out, and you have received this Claim Form because you are the spouse, adult child, representative, person with valid durable power of attorney, heir, or responsible family member of a Settlement Class Member, please note this under your printed name above by also indicating the capacity in which you are filling out the form (i.e. as spouse, adult child, representative, person with valid durable power of attorney, heir, etc.).

Questions?

Visit: www._____.com

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